Archives of Dermatology and Syphilology

VOLUME 25 MARCH, 1932 NUMBER 3

THE EFFECT OF ARSENIC ON RABBITS

MICROCHEMICAL STUDIES FOLLOWING THE ADMINISTRATION OF THE ARSPHENAMINES AND TRYPARSAMIDE *

EARL D. OSBORNE, M.D.

EDWIN D. PUTNAM, M.D.

AND

BLANCHE S. HITCHCOCK, B.S.

BUFFALO

Since the introduction of arsphenamine and neoarsphenamine by Ehrlich, information regarding the causes of accidents following their use has been sought by laboratory research and by clinical investigation. The more recent introduction of silver arsphenamine, sulpharsphenamine and tryparsamide has intensified the desire of scientists to learn more regarding the toxic and therapeutic effects of all of the organic arsenicals used in the treatment for syphilis. The use of extremely large doses of tryparsamide over long periods with almost a total lack of toxic reactions, except for the effect on the optic nerve, has led to much speculation regarding the chemical action of tryparsamide in the body and its apparent affinity for certain organs and tissues. Owing to the fact that one of us had used microchemical methods for several years for the demonstration of arsenic in tissue, particularly with reference to arsenical keratoses, arsenical pigmentation of the skin and arsphenamine dermatitis, it was felt that the employment of this method would be of value for the study of the tissue of rabbits following the administration of various arsphenamines and of tryparsamide.

During the past twenty years much work has been done from a chemical standpoint on the determination of arsenic in the various organs of the body following the administration of the arsenicals. Likewise, studies of the arsenic content of the urine and feces following the administration of the arsenicals have been made. As far back as 1884 and 1885, Chittenden and Smith [1] showed that the quantity of arsenic in the brain varied with the nature of the compound used, and that only readily soluble arsenicals penetrated the substance of the brain.

* Submitted for publication, Feb. 15, 1931.

* Read at the Fifty-Fourth Annual Meeting of the American Dermatological Association, Toronto, Canada, June, 1931.

1. Chittenden, R. H., and Smith, H. E.: Studies from the Laboratory of Physiological Chemistry, New Haven, Conn., Sheffield Scientific School, 1884-1885.

In 1914, Underhill [2] showed relatively large amounts of arsenic stored in the substance of the brain following poisoning with arsenous oxide. More recently, in 1928, Underhill and Dimick,[3] working with dogs, showed that the distribution of arsenic in the tissue following the administration of an organic arsenical, such as neoarsphenamine, differed from the distribution following an inorganic arsenical, such as arsenous acid. They demonstrated that the quantity present in the tissues did not necessarily depend on the amount given or on the number of injections. Following the therapeutic injection of neoarsphenamine, the kidneys contained the largest amount of arsenic, followed in order by the spleen, the liver, the thyroid gland, the muscle of the heart, the reproductive organs and the brain, whereas following the injection of inorganic arsenic oxide, the liver was preeminently the place of storage, followed in order by the kidneys, the spleen, the spinal cord and the brain, but the amount in the brain equaled that in the spleen. They concluded that arsenic in any form penetrates the nervous system with great difficulty. Fordyce, Rosen and Meyers [4] did a tremendous amount of work on the determination of arsenic in the various tissues and excreta following the administration of all forms of organic arsenicals. In many instances the figures that they obtained do not correspond to those of Underhill and Dimick. We have always believed that chemical analyses of the arsenic content of organs and tissues following the administration of arsenicals tell only part of the story. One cannot tell how much arsenic is present in the blood in a certain organ after death, how much blood is in that organ or how much arsenic has actually penetrated the cellular tissue of the organ. For instance, a determination of 0.5 mg. of arsenic per hundred milligrams of dried substance of the brain is not conclusive proof that any of the arsenic is in the tissue of the brain. Because of this fact, it was felt that a microchemical method that would demonstrate the actual presence of arsenic in the tissue would give considerable definite information regarding the amount and location of such arsenic and some data regarding its metabolism.

Many studies of the organs of human beings and animals following the administration of therapeutic and lethal doses of the various arsphenamines have been made from the histologic standpoint. We have gained

---

2. Underhill, F. P.: The Distribution of Arsenic in a Human Body, J. Biol. Chem. **19**:141, 1914.

3. Underhill, F. P., and Dimick, Alice: The Distribution of Arsenic in the Tissues After Serial Administration of Neoarsphenamine, Am. J. Physiol. **84**:56, 1928.

4. Fordyce, J. A.; Rosen, I., and Meyers, C. N.: Quantitative Studies in Syphilis from a Clinical and a Biological Point of View: XIV. Localization and Fate of Salvarsan, Neosalvarsan, Silver Salvarsan and Tryparsamide in the Viscera After Intravenous Administration in Rats, Am. J. Syph. **8**:377, 1924; XVI. Localization and Fate of Sulpharsphenamine in the Viscera and Its Penetration Into the Central Nervous System After Intravenous Administration in Rats, ibid. **9**:18, 1925.

much information from the researches of Ullman,[5] who used the early German brand of arsphenamine and neoarsphenamine and, more recently, from the studies of Brown [6] and those of Pearce and Brown,[7] Schamberg,[8] Kolmer [9] and their associates. The latter group of workers demonstrated conclusively that in rats arsphenamine and to a less degree neoarsphenamine administered in toxic doses produced particular damage to the blood vessels, the liver and the adrenals. Later Kolmer and Lucke [10] showed that arsphenamine, in particular, produced damage to the liver with focal necroses, whereas neoarsphenamine produced relatively less damage to the liver and considerably more damage to the kidneys. It seems to us that a microchemical method of examination that would demonstrate the arsenic in the organs and tissues would give additional information on the following points:

1. What organs take up arsenic from the blood stream? The fact that damage has been found in the adrenals following the administration of toxic or lethal doses of arsphenamine does not necessarily prove that the adrenal glands actually remove arsenic from the circulation and store it. The damage might be due entirely to the circulation of unmetabolized arsphenamine.

2. What is the difference in the metabolism of therapeutic and of lethal doses of arsphenamine and tryparsamide?

3. Do the arsphenamines and tryparsamide actually penetrate into the tissue of the central nervous system, and in what quantity?

4. What is the rôle of the gastro-intestinal tract in the elimination of arsenic? This subject has interested us since the observation of three patients who presented severe ulcerative colitis during the course of extensive arsphenamine dermatitis.

---

5. Ullman, K.: Experimentelles zur arsenwirkung auf die organe, Wien. klin. Wchnschr. **27**:838, 1914.

6. Brown, W. H.: Lesions Produced by Arsenicals and Their Bearing on the Problem of Specific Arsenic Therapy, Bull. Johns Hopkins Hosp. **26**:309, 1925.

7. Pearce, W., and Brown, W. H.: Histological Changes in Arsenic Kidneys, J. Exper. Med. **22**:525, 1915; On the Pathological Action of Arsenicals on the Adrenals, ibid. **22**:535, 1915.

8. Schamberg, J. F.: Clinical Commentary on Studies of Histologic Changes in Organs Induced by Arsphenamin, by Neo-Arsphenamin and by Mercury, Arch. Dermat. & Syph. **3**:571 (April) 1921.

9. Kolmer, J. A., and Lucke, B.: A Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, Arch. Dermat. & Syph. **3**: 483 (April) 1921; A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arsphenamin, ibid. **3**:515 (April) 1921.

10. Kolmer, J. A., and Lucke, B.: A Comparative Study of the Histologic Changes Produced Experimentally in the Liver and Kidneys of the Rat by Arsphenamin and Neo-Arsphenamin, Arch. Dermat. & Syph. **9**:321 (March) 1924.

5. What is the difference in the method of elimination of arsphenamine, and of neoarsphenamine, sulpharsphenamine and tryparsamide?

We believe that our studies have given further facts in the elucidation of these problems.

EXPERIMENTAL MATERIAL

Our experimental work was done entirely with rabbits. One series of rabbits was given eight weekly therapeutic doses of arsphenamine; another, twelve weekly therapeutic doses of tryparsamide. Forty-eight hours following the last injection, these rabbits were killed by the inhalation of illuminating gas. Another series of rabbits was given lethal doses, consisting of ten times the therapeutic dose, of neoarsphenamine, sulpharsphenamine and tryparsamide; these rabbits were killed with illuminating gas one hour following the injection. The next series of rabbits was given lethal doses consisting of ten times the therapeutic dose of neoarsphenamine, sulpharsphenamine and tryparsamide; the rabbits were killed in the same manner at the end of twenty-four hours. One other rabbit was given a lethal dose of tryparsamide consisting of ten times the therapeutic dose and was killed in the same manner at the end of forty-eight hours. Without going into detail, it may be stated that our method for computing the therapeutic and lethal doses of the various drugs was identical with that of Kolmer and Lucke.[9] Necropsy was immediately performed on the animals, and the brain, the spinal cord, the lungs, the heart, the liver, the spleen, the adrenals, the kidneys, the small intestine, the colon, the stomach and the pancreas were removed. Sections of tissue from each organ were at once placed in a diluted solution of formaldehyde, U. S. P. (1:10). Because of the labor and time involved in preparing these tissues for examination according to the method previously outlined, a more extensive program could not be undertaken, but sufficient material was covered to give us a number of definite conclusions.

METHOD

The method employed for the microchemical demonstration of arsenic in the tissue was the same as that employed by one of us (Dr. Osborne)[11] in 1925 in the study of arsenical keratoses and pigmentation and in 1928 in the study of arsphenamine dermatitis.[12] The method was first introduced by Justus[13] in 1905, and was modified by Brünauer[14] in 1921, and by one of us (Dr. Osborne)[11] in 1925. The same method for the demonstration of arsenic in tissue was also used by Memmesheimer[15] in 1928, who confirmed the work of one of us (Dr. Osborne). It is not necessary at this time to go into details regarding this method. It is slow and tedious and requires painstaking care in embedding the sections in celloidin and in the cutting. We recommend a temperature of between 70 and 75 C.

---

11. Osborne, Earl D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925.

12. Osborne, Earl D.: Microchemical Studies of Arsenic in Arsenical Dermatitis, Arch. Dermat. & Syph. **18**:37 (July) 1928.

13. Justus, J.: Ueber Arsenvergiftung auf Grund einer mikrochemisch-histologischen Methode, Dermat. Ztschr. **12**:277, 1905.

14. Brünauer, S. R.: Ueber mikrochemisch-histologischen nachgewiesenes Arsen bei Hyperkeratosis arsenicalis, Arch. f. Dermat. u. Syph. **129**:186, 1921.

15. Memmesheimer, A. M.: Der histochemische Nachweis von Arsen in der Haut bei Fällen von salvarsanlichen und Salvarsandermatitis und seine Bedeutung für die Pathogenese dieser Erkrankungen, Dermat. Ztschr. **54**:4, 1928.

for the reduction treatment with hydrogen sulphide. For the best results, sections should be cut with a thickness of not over 5 microns.

For the purposes of this study, we were particularly concerned over the ability of this method to demonstrate the arsenic of unchanged or unmetabolized arsphenamine and tryparsamide in the body of the animal. In order to settle this question, we performed several experiments:

1. A rabbit was given a lethal dose of arsphenamine and immediately killed with illuminating gas. The various organs were removed and prepared according to the method described. Crystals of arsenic trisulphide were present in large quantities in all of the blood vessels of the organs examined and to a small extent in the parenchyma of the liver and kidneys.

2. A solution of alkalinized arsphenamine ready for intravenous administration was subjected to reduction treatment with hydrogen sulphide. A precipitate characteristic of arsenic trisulphate was formed, and microscopic examination of this precipitate confirmed the impression. Neoarsphenamine, sulpharsphenamine and tryparsamide gave the same results.

3. Twenty-five cubic centimeters of blood was withdrawn from a patient immediately following the completion of an intravenous injection of a therapeutic dose of arsphenamine. The cellular elements were removed by centrifugation, and the plasma was submitted to the hydrogen sulphide process at a temperature of 56 C. A gross and microscopic examination of the precipitate showed that it was arsenic trisulphide.

Carlson [16] showed that under the chemical conditions that existed, if arsenic was present, it must be precipitated as trisulphide. He demonstrated that, although arsenic trisulphide precipitates more readily in an acid solution, it also precipitates in a neutral solution if it is incubated long enough at from 70 to 80 C. Arsenic trisulphide is precipitated from solutions of an arsenate as well as from those of an arsenite, since the hydrogen sulphide gradually reduces the arsenate to an arsenite.

In view of this chemical and experimental evidence, we felt justified in assuming that in the tissues of the rabbit examined any arsenical that was present would be precipitated as arsenic trisulphide.

A new histochemical method for the demonstration of arsphenamine in the tissues was published in 1928 by von Jancsó, Jr.[17] The process depends on the reduction of an ammoniacal silver nitrate solution by arsphenamine. Schumacher [18] at once pointed out that von Jancsó's method was not new, but that it was essentially the same as that which had been used in the demonstration of spirochetes in tissue. He also pointed out that von Jancsó's method demonstrated the unchanged

16. Carlson, C. E.: Eine neue Methode zum leichten Nachweis und zur raschen Ausscheidung von Arsen und gewissen Metallsalzen aus Flüssigkeiten, Ztschr. f. physiol. Chem. **68**:243, 1910.

17. von Jancsó, N., Jr.: Eine neue histochemische Methode zur biologischen Untersuchung des Salvarsan und verwandter Arsenobenzolderivate, Ztschr. f. d. ges. exper. Med. **61**:63, 1928.

18. Schumacher, J.: Salvarsanwirkung und Retikuloendothel, Dermat. Ztschr. **53**:569, 1928.

arsphenamine in the body and therefore that it was of little use in a study of the metabolism, the storage and the elimination of the arsenicals.

RESULTS OF EXPERIMENTS

Examination of Tissues of the Rabbit Removed at Necropsy Two Days After Completion of a Course of Eight Therapeutic Injections of Arsphenamine.—A detailed study of the brain, the cord, the lungs, the heart, the liver, the spleen, the adrenals and the kidneys showed only a smattering of arsenic, except in the liver where a small amount was seen. We could not detect any particular localization of the arsenic in the liver. There seemed to be as much at the center of the lobule as at the periphery. It is unfortunate that the tissue removed from the stomach, the small intestine and the colon was accidently destroyed. In view of our observations following the administration of lethal doses of the various arsenicals, we believe that a moderate amount of arsenic would have been found in the intestinal tract, particularly in the colon. In all of the organs except the liver, the little amount of arsenic that was seen was in the smaller blood vessels and capillaries. No arsenic could be found in the parenchyma of the organs examined. A repetition of this experiment gave essentially the same results. From our observations in rabbits receiving a course of therapeutic doses of arsphenamine, we made the following conclusions: 1. The drug is rapidly metabolized in the liver and rapidly excreted. 2. No evidence was present that in healthy rabbits receiving eight therapeutic doses of arsphenamine, the storage of arsenic in any organ is a major consideration. Underhill and Davis [19] showed that after each injection of neoarsphenamine and arsphenamine into dogs, there was a greater elimination of arsenic the second day after injection and a larger amount excreted and a larger percentage of excretion before the next injection. Later, Underhill and Dimick [8] showed that in dogs there was no essential difference in the arsenic content of the various organs, after one or several injections of neoarsphenamine had been made. Our experiment confirms this observation in rabbits and, in addition, emphasizes the lack of storage.

Examination of Tissues of the Rabbit Removed at Necropsy Twenty-Four Hours After a Lethal Dose of Arsphenamine.—No arsenic was seen in the brain or the adrenals. The spinal cord showed an occasional crystal of arsenic. The lungs were edematous; the blood vessels were greatly dilated and contained many thrombi. A small amount of arsenic was found around the smaller blood vessels and an occasional crystal in the pulmonary tissue. Occasionally a crystal of arsenic was found in

19. Underhill, F. P., and Davis, S. H.: Excretion of Arsenic After Serial Administration of Arsphenamin and Neo-Arsphenamin, Arch. Dermat. & Syph. **5**: 40 (Jan.) 1922.

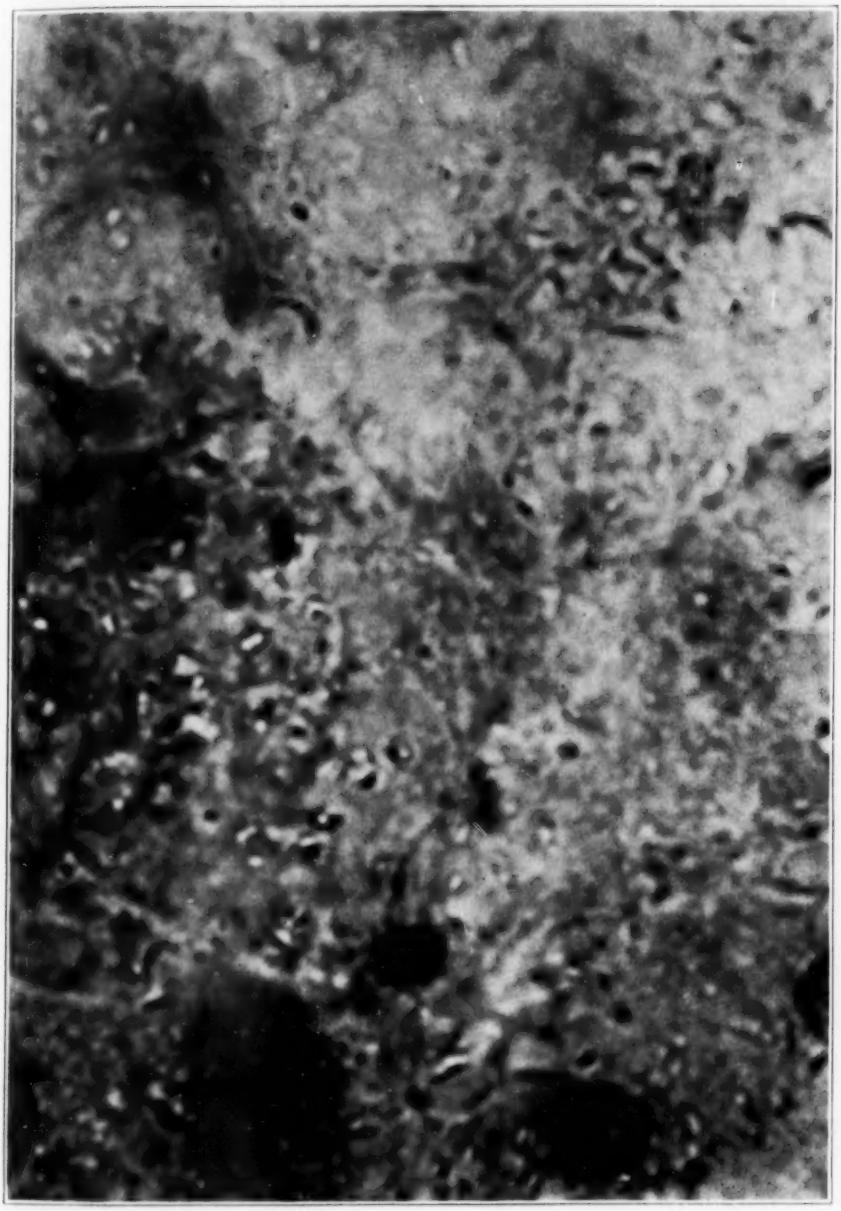


Fig. 1.—Crystals of arsenic trisulphide in maximum amount in the liver of a rabbit twenty-four hours after a lethal dose of arsphenamine; × 3,800.

the heart. The liver (fig. 1) showed a maximum amount of arsenic, whereas the glomeruli and tubules of the kidneys showed only a small amount. The stomach, the small intestine and the colon were again destroyed accidentally. The following conclusions were made from this experiment: 1. Twenty-four hours after the administration of a lethal dose of arsphenamine, the liver contains a maximum amount of arsenic, indicating an attempt on the part of the liver to metabolize the arsphenamine as rapidly as possible, up to the limit of its ability and in spite of any damage that might have occurred from the circulation of an overwhelming amount of arsphenamine. 2. The kidneys either played a minor rôle in the elimination of arsenic following the administration of a lethal dose of arsphenamine or they were damaged by the overwhelming dose of neoarsphenamine to the point at which they could no longer function properly. 3. There was no apparent storage of arsenic in any of the organs other than the liver.

Examination of Tissues of the Rabbit Removed at Necropsy Twenty-Four Hours After a Lethal Dose of Neoarsphenamine.—The tissue of the brain showed no arsenic. The tissue of the spinal cord immediately around the central canal and the adjacent arterioles showed a moderate amount of crystals of arsenic. The lungs contained little arsenic, except in and around the smaller blood vessels. The heart contained no arsenic. All parts of the lobule of the liver were loaded with arsenic. The spleen contained little arsenic, except immediately around the smaller blood vessels and in the septums of the connective tissue. The adrenals showed an occasional small group of crystals of arsenic around some of the smaller blood vessels, but none was found in the tissue of the adrenal glands. All parts of the kidneys showed relatively small amounts of arsenic. There was marked degeneration of the epithelium of the tubules. The stomach contained considerable arsenic, both in the mucosa and throughout the muscular layers. Practically no arsenic was seen in the pancreas. The following conclusions were made from this experiment: 1. At the end of one hour following the injection of a lethal dose of neoarsphenamine, the liver was making a maximum attempt to metabolize the arsphenamine. 2. The kidneys play a minor rôle in the elimination of the arsenic. 3. The intestinal tract, including the stomach, the small intestine and the colon, was the greatest factor in the elimination of the arsenic. 4. None of the other organs was a factor in the storage of arsenic, except when it occurred in and around the smaller blood vessels.

Examination of Tissues of the Rabbit Removed at Necropsy Twenty-Four Hours After a Lethal Dose of Neoarsphenamine.—No arsenic was found in the brain, the cord, the lungs or the heart. An occasional crystal of arsenic was seen around the smaller blood vessels in the spleen

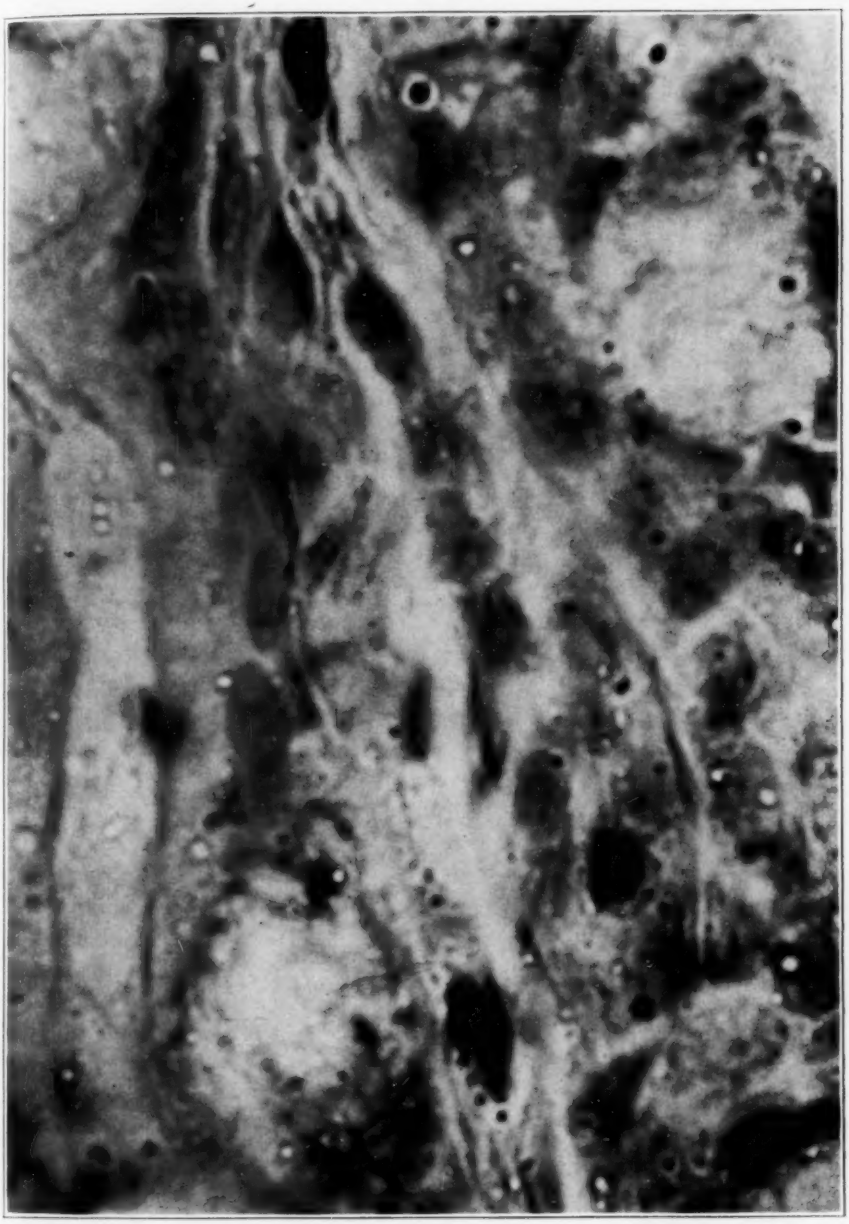


Fig. 2.—Crystals of arsenic trisulphide in maximum amount in the mucosa of the colon twenty-four hours after the injection of a lethal dose of neoarsphenamine; × 3,800.

and pancreas. The liver contained considerable arsenic, though not so much as at the one hour interval. The tubules and glomeruli of the kidneys showed a large amount of arsenic. The muscular layers of the stomach showed a moderate amount of arsenic; the submucosa, a small amount, and the mucosa, almost none. A maximum amount of arsenic was contained in the muscular layers and in the mucosa of the small intestine. The colon also showed the same amount (figs. 2 and 3). The following conclusions were made from this experiment: 1. Twenty-four hours following the administration of a lethal dose of neoarsphenamine the liver is still able to metabolize the drug, and the arsenic is being eliminated rapidly through the intestinal tract and, to a somewhat less extent, through the kidney. 2. Arsenic was also found in or around the smaller blood vessels; none was stored in the parenchyma of the organs.

Examination of Tissues of the Rabbit Removed at Necropsy One Hour After a Lethal Dose of Sulpharsphenamine.—An occasional crystal of arsenic was seen in the brain. The spinal cord showed a small amount, especially around the central canal and the adjacent arterioles. The liver showed marked degenerative changes and little arsenic. The spleen showed many thrombi, and there was a small amount of arsenic in the pulp of the spleen. A small amount of arsenic was present around some of the smaller blood vessels in the medulla and cortex of the adrenals. The kidneys were practically devoid of arsenic, except around some of the smaller blood vessels in the medulla and pelvis of that organ. Except for a slight amount around the small blood vessels in the submucosa, the small intestine and colon showed no arsenic. The stomach showed no arsenic. From this experiment we made the following conclusions: 1. At the end of one hour following a lethal dose of sulpharsphenamine, the liver has been overwhelmed by the large dose of a vasculotoxic drug. The liver is unable to metabolize the drug in sufficient quantities to show in the organs of excretion, namely, the kidneys, the stomach, the small intestine and the colon. 2. Since the liver is unable to metabolize the sulpharsphenamine, it is fair to assume that the other organs of the body are exposed to vascular damage. 3. In comparing sulpharsphenamine and neoarsphenamine at the one hour interval following the administration of a lethal dose, the evidence clearly indicated a more rapid metabolism of neoarsphenamine with its subsequent elimination through the organs of excretion.

Examination of Tissues of the Rabbit Removed at Necropsy Twenty-Four Hours After a Lethal Dose of Sulpharsphenamine.—The brain, cord, heart, lungs, spleen, adrenals, small intestine, stomach and pancreas showed no arsenic. The liver showed advanced degenerative stages and contained a large amount of arsenic. As to the excretory organs, the kidneys showed only a small amount of arsenic, and the colon a moderate

Fig. 3.—Crystals of arsenic trisulphide in maximum amount in the muscles of the colon of a rabbit, twenty-four hours after a lethal injection of neoarsphenamine; × 3,800.

amount. From this experiment we made the following conclusions: 1. The liver had been damaged to a point at which metabolism of the arsphenamine was carried on at only a slow rate, as evidenced by the negligible quantity of arsenic found in the organs of excretion. 2. In spite of the inability to metabolize the arsphenamine into a form in which it could be excreted, none of the other organs stored arsenic. This observation indicates that sulpharsphenamine, as such, is not in chemical form suitable for penetration into the parenchyma of the various organs.

Examination of Tissues of the Rabbit Removed at Necropsy Forty-Eight Hours After Completion of a Course of Twelve Therapeutic Injections of Tryparsamide.—In some portions of the brain there was a moderate amount of arsenic, whereas in other parts it was almost totally absent (fig. 4). There did not seem to be a preponderance of arsenic in either the gray or the white matter. This was the first time we had found an appreciable amount of arsenic deposited in the parenchyma of the central nervous system. The spinal cord showed little arsenic. The lungs, the heart, the liver and the adrenals contained no arsenic that we could demonstrate. The spleen showed a moderate amount, but it was not uniformly distributed. The tubules and glomeruli of the kidneys showed a small amount of arsenic. From this experiment we made the following conclusions: 1. A course of therapeutic injections of tryparsamide causes arsenic to be taken up by the central nervous system, as shown by the moderate amount in the brain and a small amount in the spinal cord. It is interesting to speculate on how much arsenic would appear in the central nervous system if a course of fifty injections had been given. 2. Either the tryparsamide is excreted as such or it requires little metabolizing in the liver. 3. Since the kidneys showed only a small amount of arsenic, it is evident that most of it had been excreted before the death of the animal. This observation is in accord with chemical studies on the rate of excretion of tryparsamide.

Examination of Tissues of the Rabbit Removed at Necropsy One Hour After a Lethal Dose of Tryparsamide.—Both the gray and the white matter of the brain showed scattered small groups of crystals of arsenic, especially around the smaller blood vessels. The cord showed a small amount of arsenic near the anterior fissure around some of the smaller blood vessels and in the region of the central canal. The liver contained only a small amount of arsenic. The spleen contained a moderate amount of arsenic, which seemed to be in proportion to the amount of blood present. The adrenals did not show arsenic. The kidneys contained a rather large amount of arsenic, particularly in the glomeruli and in the proximal loops of the tubules. Almost none was seen in the pelvis of the kidney. The blood vessels of the kidneys contained a large amount of arsenic. All of the coats of the small intestine

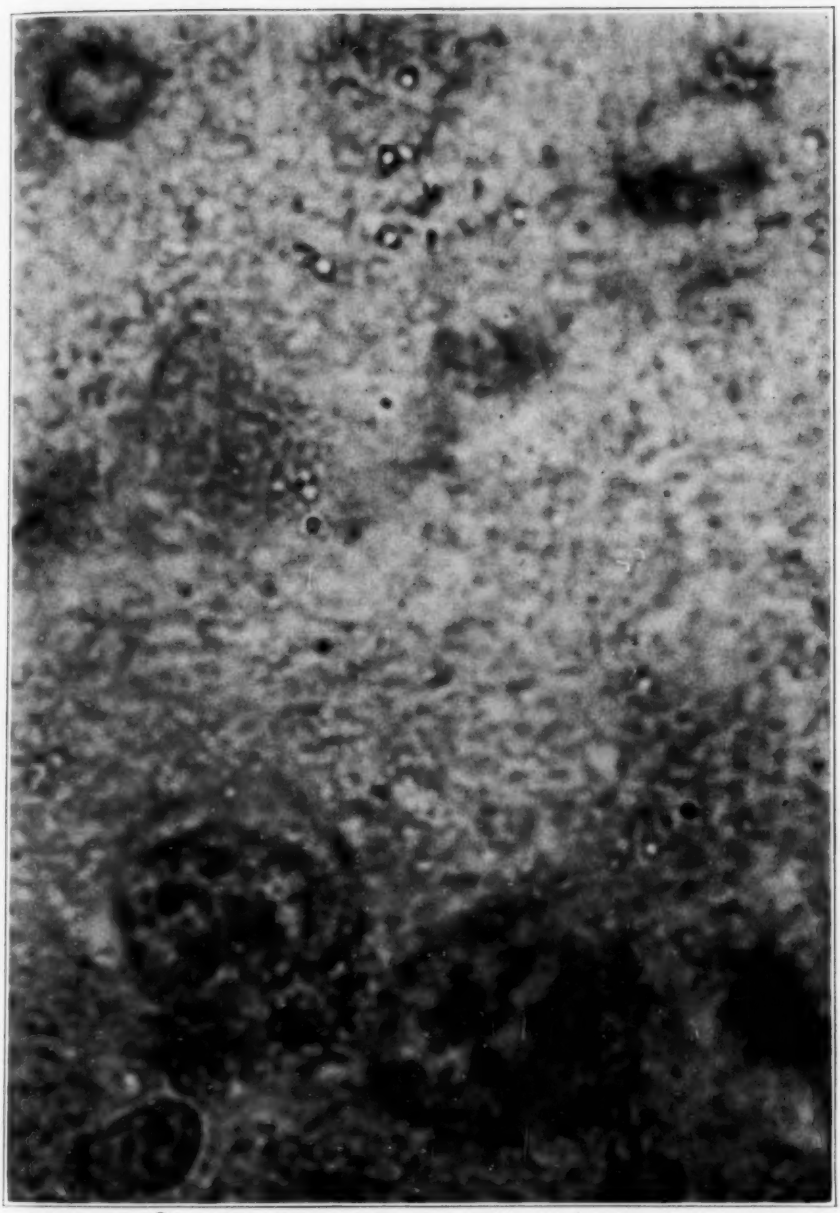


Fig. 4.—Crystals of arsenic trisulphide in moderate amount in the brain of a rabbit, forty-eight hours after the completion of a course of twelve therapeutic injections of tryparsamide; × 3,800.

showed a small amount of arsenic, especially around some of the smaller blood vessels. The stomach showed a maximum amount of arsenic; it was scattered throughout the entire thickness of the walls (fig. 6). The colon contained more arsenic than the stomach. For the first time we observed a considerable quantity of arsenic in the cross-sections of the ganglion of a sympathetic nerve (fig. 5). From this experiment we made the following conclusions: 1. At the end of one hour following a lethal dose of tryparsamide some arsenic has already penetrated into the

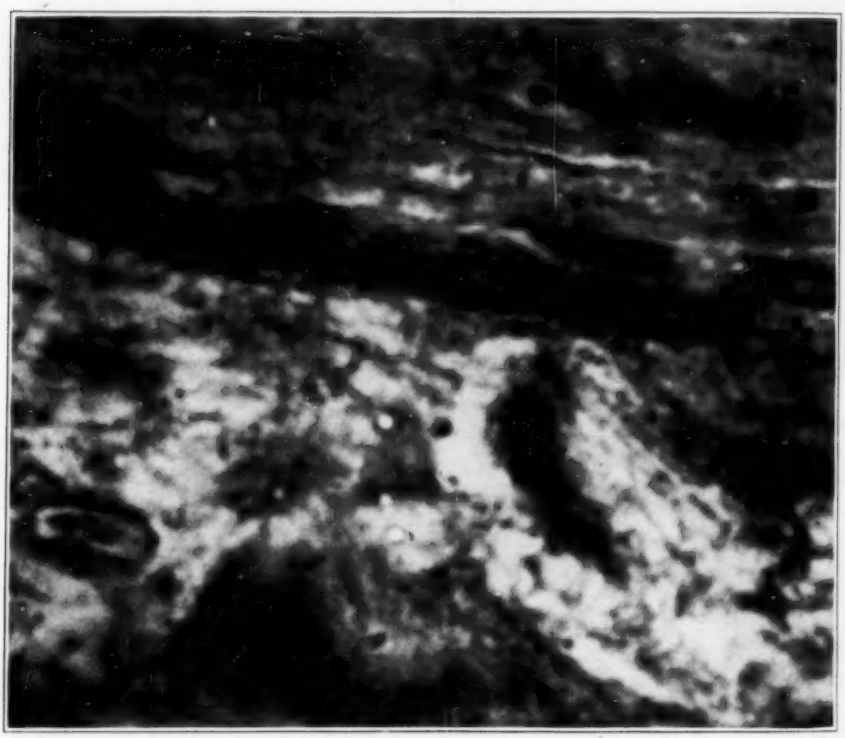


Fig. 5.—Crystals of arsenic trisulphide seen for the first time in a cross-section of a ganglion of a sympathetic nerve just outside the longitudinal muscle of the colon. The rabbit had received a lethal dose of tryparsamide one hour before death; × 3,800.

central nervous system. 2. The liver is evidently a neglible factor in the metabolism of the drug. 3. The tryparsamide is rapidly excreted through the kidneys and the entire intestinal tract.

Examination of Tissues of the Rabbit Removed at Necropsy Twenty-Four Hours After a Lethal Dose of Tryparsamide.—No arsenic was found in the brain, cord, lungs, heart, spleen or adrenals. The liver contained a moderate amount, and there were evidences of moderate degen-

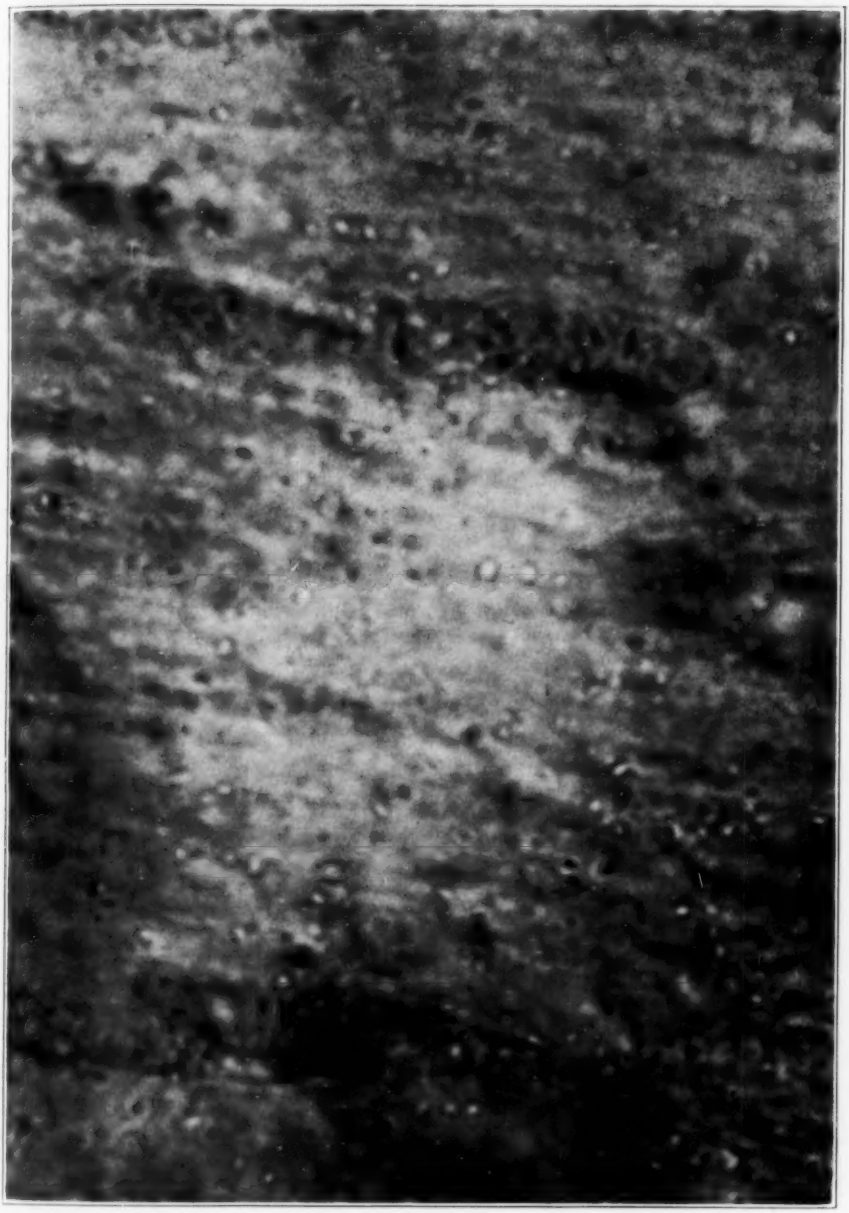


Fig. 6.—Crystals of arsenic trisulphide in maximum amount in the muscle of the stomach of a rabbit, one hour after the administration of a lethal dose of tryparsamide; × 3,800.

erative changes. The organs of excretion showed a small amount in the kidneys, small intestine and the stomach and a large amount in the colon. From this experiment we made the following conclusions: 1. At the end of twenty-four hours following the administration of a lethal dose of tryparsamide, the liver has begun to show degenerative changes with retention of arsenic. 2. Since the excretory organs show less arsenic than at the one hour interval, most of the arsenic must have been eliminated.

Examination of Tissues of the Rabbit Removed at Necropsy Forty-Eight Hours After a Lethal Dose of Tryparsamide.—At the end of forty-eight hours following the administration of a lethal dose of tryparsamide the brain contained a moderate amount of arsenic, which was scattered throughout the white and the gray matter. The cord likewise contained a moderate amount of arsenic. No arsenic was found in the lungs, the heart or the adrenals. The liver showed a maximum amount of arsenic with considerable cloudy swelling, edema and degeneration of the cells of the liver. The glomeruli and tubules of the kidneys showed a moderate amount of arsenic. From this experiment we drew the following conclusions: 1. The liver takes up an increasing quantity of arsenic following the administration of a lethal dose of tryparsamide. 2. It seemed to us that the amount of arsenic was in proportion to the degree of degeneration of the cells of the liver. On comparing the amount of arsenic found in the liver forty-eight hours after a lethal dose with that found in the liver forty-eight hours after the completion of a therapeutic course, we found that the liver contained a maximum amount of arsenic in the first instance, whereas in the latter instance none could be found. After a lethal dose of tryparsamide either the excessive arsenic was stored in the liver and produced damage because of this storage or the liver was damaged from the circulating arsenical and consequently retained arsenic in increasing quantities. In view of the observation in previous experiments, that the liver was a negligible quantity in the metabolism of tryparsamide, we were inclined to the belief that the increasing retention of arsenic following a lethal dose of tryparsamide was secondary to the degenerative changes.

COMMENT

We offer the foregoing experiments as the first installments of a comprehensive and as yet incomplete study of the microchemistry of the arsenicals. There are many leads that must be followed before absolute conclusions can be reached. These experiments must be repeated with other animals, additional drugs and other methods of administration. Other organs, such as the skin, bladder, peripheral nerves and bones, must be studied. A detailed study of the vascular effects would be

exceedingly valuable in view of the fact that arsphenamines are judged largely by their vasculotoxic qualities. Complete necropsy material from human beings is indispensable. A study of the effect of feeding and fasting, fever and diseases of the liver would be pertinent. Further experiments with long courses of therapeutic doses of tryparsamide are indicated.

The observations in regard to the intestinal tract are exceedingly important and interesting from a pharmacologic point of view. Pharmacologists have long taught that the small and large intestines excrete arsenic in a trivalent form after reduction in the liver. In 1929, however, Bargen, Osterberg and Mann,[20] working with an isolated colon in

A Rough Tabulation of the Results of Microchemical Studies of Tissues of the Rabbit Following Therapeutic and Lethal Doses of Arsphenamine, Neoarsphenamine, Sulpharsphenamine and Tryparsamide *

	Arsphenamine						Tryparsamide			
	Therapeutic, 48 Hrs. After Last Dose	Lethal, 24 Hours	Neoarsphenamine Lethal, 1 Hour	Neoarsphenamine Lethal, 24 Hours	Sulpharsphenamine Lethal, 1 Hour	Sulpharsphenamine Lethal, 24 Hours	Therapeutic, 48 Hrs. After Last Dose	Lethal, 1 Hour	Lethal, 24 Hours	Lethal, 48 Hours
Organ										
Brain	—	—	—	—	Occ.	—	++	+	—	++
Cord	—	Occ.	Occ.	—	+	—	+	+	—	++
Lung	—	Occ.	Occ.	—	—	—	—	—	—	—
Heart	—	—	—	—	—	—	—	—	—	—
Liver	+	++++	++++	++++	+	++++	—	+	++	++++
Spleen	—	—	+	Occ.	+	—	++	++	—	—
Adrenals	—	—	+	—	Occ.	—	—	—	—	—
Kidney	—	+	+	++++	Occ.	+	+	+++	+	++
Small intestine	..	..	+	++++	—	—	..	+	+	..
Colon	..	..	++++	++++	—	++	..	++++	+++	..
Stomach	..	..	++	++	—	—	..	++++	+	..
Pancreas	..	..	+	..	—	—	..	+	—	..

* Key: +, small amount of arsenic; ++, moderate amount of arsenic; +++, large amount of arsenic; ++++, maximum amount of arsenic.

dogs, came to the conclusion that the neoarsphenamine (trivalent) and meta-amino-para-oxyphenyl arsonic acid (pentavalent) were absorbed freely from the colon but were not excreted into it. We have never seen greater quantities of arsenic in any organ or tissue than in the stomach, the small intestine and the colon in these experiments. When the arsenic has been found in the mucosa, we have found it throughout the layers of muscle. At times we found arsenic in the layers of muscle and not in the mucosa. The presence of arsenic in the stomach certainly favors the theory of excretion, at least in that part of the intestinal tract. The presence of arsenic throughout all the muscular layers of the entire intestinal tract strongly suggests excretion rather than absorption. However, these observations do not disprove the theory of absorption in the colon.

20. Bargen, J. A.; Osterberg, A. E., and Mann, F. C.: Absorption and Excretion of Arsenic, Bismuth, and Mercury: Experimental Work on the Colon, Am. J. Physiol. **89**:640, 1929.

Before this question can be answered, microchemical observations of the colon following the rectal administration of the arsenicals must be available. For the purpose of this paper and until further evidence is adduced, we have interpreted our observation of arsenic in all layers of the intestinal tract as arsenic in the process of excretion. In 1928, Brown [21] stated that Clausen and Jeans [22] had shown arsenic evenly distributed in the walls of the intestine. As a matter of fact, Clausen and Jeans, working with kittens, showed appreciable amounts of arsenic in the walls of the stomach, duodenum, ileum, colon and rectum after the administration of arsphenamine. As far as we can determine, we are the first to demonstrate arsenic in the muscular layers and the mucosa of the intestinal tract.

CONCLUSIONS

A rough tabulation of the foregoing results is shown in the accompanying table. Certain general conclusions seem indicated.

1. Arsphenamine given to rabbits in therapeutic doses is rapidly metabolized and eliminated, with no evidence of appreciable storage.

2. No appreciable amount of arsenic is found in the parenchyma of the central nervous system of rabbits after the administration of arsphenamine, neoarsphenamine or sulpharsphenamine.

3. Following the administration of therapeutic and lethal doses of tryparsamide to rabbits, the parenchyma of the brain and spinal cord shows appreciable quantities of arsenic.

4. The adrenals are not storehouses for arsenic. If damage is done, it is due to vascular damage caused during the period of circulation of the unmetabolized arsphenamine.

5. The lack of any appreciable storage of arsenic in any of the organs, except the liver and the organs of excretion, suggests that most of the drug is in the vascular system prior to metabolism in the liver.

6. In comparing the observation following the administration of arsphenamine, neoarsphenamine and sulpharsphenamine, the evidence points to neoarsphenamine as being the least toxic, since it is present in the liver in large quantities at one hour and at twenty-four hours following a lethal dose, and it is being metabolized in sufficient quantities to appear in maximum amount in the organs of excretion. Sulpharsphenamine appears to be the most toxic. At the one hour interval, following a lethal dose, something has occurred to prevent the liver from metabolizing the drug. No sulpharsphenamine appears in the organs of excretion, and little is found in the liver. At the end of twenty-four hours the

21. Brown, P. W.: Treatment of Endomebiasis, Ann. Int. Med. **11**:177, 1928.

22. Clausen, S. W., and Jeans, P. C.: The Distribution of Arsenic After Intravenous Administration of Arsphenamine in Children, Am. J. Syph. **6**:556, 1922.

liver contains a maximum amount of arsenic, but the organs of excretion contain relatively little.

7. In lethal doses, tryparsamide apparently requires little or no metabolizing in the liver, but is excreted rapidly by the kidneys and the entire intestinal tract. Over a period of forty-eight hours after the administration of a lethal dose, the liver takes up an increasing amount of arsenic the amount of which seems to parallel the degree of damage to the liver.

8. A discussion of the observation of arsenic in all of the layers of the intestinal organs is given.

ABSTRACT OF DISCUSSION

DR. J. FRANK SCHAMBERG, Philadelphia: I am stimulated to discuss this paper by the admirable work that has been carried out by Dr. Osborne and his associates. As you will readily perceive, there is much in this paper that harmonizes with our clinical concept of the remedies referred to and their mode of action. Dr. Osborne has stated that tryparsamide has been shown by the method employed by him to penetrate the brain readily. This we should expect, because tryparsamide, like the other pentavalent arsenicals, is a crystalline substance that readily passes through animal membranes, whereas the arsphenamines are in the nature of colloids, and for that reason possibly they do not permeate or do so imperfectly.

The work of Kolmer and my associates has shown the effect of toxic doses of the organic arsenicals on the liver. In animals there is cellular necrosis, and I have no doubt that some of the pictures Dr. Osborne showed containing liver cells that are broken down and exhibit crystals of arsenic are evidence of this necrosis. In regard to the various brands of arsphenamine, it is surprising that although they have been in use for twenty years, there is so little agreement as to what their fate is in the body. Whether one considers the immediate reactions, the gastro-intestinal, the cutaneous or cerebral effects, there is absolute discord in the opinion of the best physicians as to what causes such accidents. We do not know the cause of these reactions, and it will be some time before we find out the cause, for we know very little about the fate of the arsphenamines in the body. Voegtlin and Smith stated that they are converted into arsenoxide, but the views of certain other physicians are not in harmony with this. We need work of the character of Dr. Osborne's to throw light on what happens to the arsenic in the system. I have long held the opinion that the action of the arsphenamines that could not be explained by faulty preparation or a faulty drug were due to some idiosyncrasy, and rested on some aberrance in the catabolism of the arsenic in the liver. Arsenic may undergo reduction, and in the liver, which is somewhat different from the other organs, the arsenic may undergo oxidation, or complete change, with a splitting-off of arsenic from the benzene ring.

It is work of the kind presented that helps us to understand what happens to these important drugs after they are introduced into the body. We know that from within one to three hours practically no arsphenamine is found in the blood. Where has it gone? Much of it is eliminated through the kidneys and bowels, and considerable amounts are deposited in the liver, in the muscles, in the spleen and elsewhere, but this does not account for the entire amount introduced into the body.

DR. WILLIAM A. PUSEY, Chicago: I wish to assure Dr. Osborne that lack of free discussion means only that such a contribution is not as easy to discuss as the usual therapeutic propositions. I said to Dr. Lane, as I have said before on hearing Dr. Osborne's contributions, that I still enjoy the clinical papers, but I like to hear papers like Dr. Osborne's, and to feel that some among us are capable of exploring the extremely intricate fields of new chemistry and physics.

DR. KARL G. ZWICK, Cincinnati: After Dr. Osborne had shown us in a previous investigation how effectively sodium thiosulphate aids the elimination of arsenic in certain disturbances following the introduction of arsphenamines, we heard from him today that in many instances the thiosulphate may actually arrive after some of the structures are damaged by the circulating arsphenamines previous to their metabolism. This prompts me to ask Dr. Osborne what prophylactic measures he suggests to obviate these early damaging effects of the arsphenamines?

DR. JOHN E. LANE, New Haven, Conn.: I should like to know whether these studies on tryparsamide have shown any explanation for the subjective eye symptoms that occur after the administration of tryparsamide.

DR. EARL D. OSBORNE, Buffalo: Answering Dr. Lane's question first: In this study we did not particularly focus our attention on the optic nerves, but that subject is now receiving attention. I should be grateful for necropsy material from persons who die very shortly after the administration of a series of injections of tryparsamide and whose optic nerve has been damaged. Naturally, that material is very difficult to get at the right time. The drug is excreted rapidly; however, we are anxious to get such material for study. Only by studying necropsy material from human beings can we arrive at any decision. As indicated in one of the slides, the presence of arsenic in the sympathetic nerve ganglion in the colon leaves no doubt that pentavalent arsenic has an affinity for the central nervous system.

In the previous paper that we published on the subject of arsphenamine dermatitis, it was shown conclusively that although the administration of sodium thiosulphate markedly hastens the elimination of arsenic, by the time sodium thiosulphate is administered the damage from the arsenic has already taken place. If one is a few hours or days too late in the administration of sodium thiosulphate, I do not believe that giving a ton of it will hasten the resolution of the arsphenamine dermatitis to any degree. Although the arsenic may disappear from the tissues very rapidly, the damage has been done.

We shall continue our studies and report again in the future.

CHEILITIS AND STOMATITIS FROM ST37 TOOTHPASTE *

H. J. TEMPLETON, M.D.
AND
C. J. LUNSFORD, M.D.
OAKLAND, CALIF.

Instances of cheilitis and stomatitis resulting from the use of toothpastes and mouth washes have been reported in the past; for instance, the Odol dermatitis mentioned by Jadassohn. When a new dentifrice is introduced to the public and when several instances of irritation from its use are seen in one office shortly thereafter, a report of such cases would seem to be in order. ST37 toothpaste is a new toothpaste being introduced by Sharp and Dohme, which is supposed to contain hexylresorcinol solution. The succeeding instances of irritation following its use were seen in the short time of two months.

REPORT OF CASES

CASE 1.—Miss V., a nurse, aged 20, consulted us on Feb. 24, 1931, because of severe cheilitis and circumoral dermatitis of two days' duration. Her history disclosed the fact that she had begun the use of ST37 toothpaste about two weeks previously. No other new preparations had been used on the lips. The eruption began as an inflammation of the lips and rapidly extended to the skin around the lips and onto the chin. The tissues were quite swollen and edematous. Itching and burning were present. After the use of the toothpaste was discontinued, the eruption rapidly retrogressed under the application of cool boric acid compresses and entirely disappeared in ten days.

We applied a patch test of the ST37 toothpaste to the flexor surface of one forearm and pure hexylresorcinol ST37 to the other arm. These were left on for twenty-four hours. When the patches were removed, a moderate dermatitis was observed at the site of contact with the toothpaste. The eruption gradually increased in intensity until it presented the reaction shown in figure 1. A similar positive reaction occurred following a patch test with pure hexylresorcinol ST37 (fig. 2).

CASE 2.—G., aged 40, a physician, consulted us on Feb. 24, 1931, because of extreme swelling of both lips and the contiguous oral mucosa. Ten days prior to the onset of the eruption he had begun the use of ST37 toothpaste. No history could be obtained of the use of other possible irritants. Prompt recovery followed the cessation of the use of the toothpaste plus subfractional doses of x-rays.

Patch tests for ST37 toothpaste and pure hexylresorcinol ST37 were applied to the forearms. Twenty-four hours after the application of the toothpaste, a

* Submitted for publication, May 12, 1931.

moderate amount of dermatitis had developed where it had been applied. The eruption gradually increased in intensity. Three days after the application of the pure hexylresorcinol ST37, a moderate dermatitis appeared. Two months after the original attack, the patient experimentally used the ST37 toothpaste one time. Three days later an acute attack of cheilitis occurred.

Case 3.—Miss B, aged 36, a teacher, consulted us on March 5, 1931, because of an acute cheilitis and circumoral dermatitis of one month's duration. The disorder had begun a few days after she had used ST37 toothpaste. We could

Fig. 1 (case 1).—Dermatitis resulting from patch test with ST37 toothpaste.

obtain no history of other possible irritants, such as new lipsticks or other cosmetics. As in our two previous cases, the eruption disappeared rapidly when the use of this toothpaste was discontinued. Patch tests gave negative reactions to pure hexylresorcinol ST37 and to all the other cosmetics that she used, but strongly positive ones to ST37 toothpaste (fig. 3). It will be noted that the dermatitis appeared under the zinc oxide adhesive lateral to the site of application of the toothpaste. We interpreted this as due to a diffusion of the substance out under the tape. We ran control tests on the other forearm with zinc oxide tape alone and obtained no reaction.

Case 4.—Donald M., a University of California student, consulted us because of a severe swelling of both lips which began after the use of a new toothpaste,

ST37, for four days. The swelling rapidly disappeared when the use of the offending toothpaste was discontinued.

A patch test of ST37 toothpaste was applied to the right forearm. This was left on over night. No reaction was visible in twenty-four hours and forty-eight hours, but at the end of three days, itching and dermatitis appeared and increased to a strongly positive reaction on the fourth day.

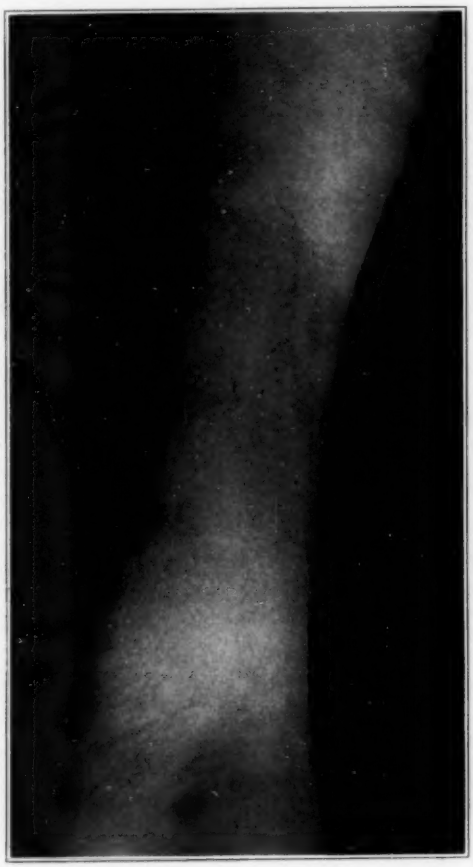


Fig. 2 (case 1).—Dermatitis resulting from patch test with pure ST37.

The patient suggested that the cheilitis might have been caused by some inter-reaction between the new toothpaste and the one he had used previously. Therefore, he applied a mixture of Listerine toothpaste and ST37 toothpaste to his left forearm and secured the same type of reaction as when ST37 toothpaste was used alone. Several weeks after recovering from his original attack, he experimentally resumed the use of ST37 toothpaste. In three days the eruption recurred.

CASE 5.—Mrs. Donald M., the wife of the preceding patient, was not seen by us. Her husband reported the following history: She had noted an irritation of her lips similar to her husband's when she had begun the use of ST37 tooth-

paste. When she discontinued its use, she promptly recovered. Later, at her husband's suggestion, she experimentally used the same toothpaste several times on Thursday and Friday. By Sunday morning her lips, gums and palatal mucous membranes were swollen and reddened. This reaction again disappeared when she stopped the use of the offending toothpaste.

Case 6.—Miss Irma H., aged 31, began the use of hexylresorcinol solution ST37 as a mouth wash (one teaspoonful to a glass of water) about Jan. 15, 1931. This was used regularly for six weeks with no resulting irritation. About February 15, she began to use ST37 toothpaste. About two weeks later her lips

Fig. 3 (case 3).—Dermatitis resulting from patch test with ST37 toothpaste.

began to burn and swell. There was also a swelling of the mucous membranes inside of the lips. A dentist eliminated the possibility of trench mouth. There had been no changes in the cosmetics that she used. Two weeks after the onset of the cheilitis she stopped the use of the ST37 toothpaste. The cheilitis then began to improve and had disappeared within two weeks.

Patch tests of pure hexylresorcinol ST37 and of ST37 toothpaste were applied on April 6. On April 7, there was no reaction to either test. On April 10, there was a strongly positive reaction to the ST37 toothpaste. There was no reaction to pure hexylresorcinol ST37.

COMMENT

The inflammation of the lips and mouths of all of the patients mentioned came on shortly after they had begun the use of a new toothpaste (ST37). In all of the patients the reaction was very severe, the lips and contiguous oral mucosa being markedly edematous. A circumoral dermatitis was also present. When the use of the offending toothpaste was discontinued, the inflammation disappeared.

Contact or patch tests were made on all three patients to test for cutaneous sensitivity to ST37 toothpaste. The toothpaste itself was applied to the flexor surface of one forearm and pure hexylresorcinol ST37 was applied to the flexor surface of the other forearm. All of the areas to which the toothpaste was applied responded by the production of a definite dermatitis. Two of the patients reacted to pure hexylresorcinol ST37. A control experiment consisted in the application of the toothpaste to the skins of volunteers who had never come in contact with it previously. No dermatitis was produced in these controls. Hexylresorcinol ST37 was used in full strength on many patients in our daily practice for over a year without producing any instances of dermatitis.

We wished to test our patients against the various ingredients used in preparing the toothpaste, such as the oils, talcs, soaps, etc. We wrote the manufacturers requesting their cooperation in this matter but they failed to furnish us with the different constituents of the toothpaste. Without such tests, one is unable to state to which particular ingredient the patients had become sensitized. The offending substance might be hexylresorcinol ST37 or any other ingredient. Or the irritation might have been caused by hexylresorcinol ST37 that had been altered chemically when incorporated in the toothpaste.

CONCLUSIONS

Six cases of cheilitis acuta following the use of ST37 toothpaste are reported. We could not demonstrate which ingredient was responsible but suspected the altered or unaltered hexylresorcinol ST37.

LXI.—LIPIDS OF THE SKIN

SOME CHANGES IN THE LIPIDS OF THE EPIDERMIS DURING THE PROCESS OF KERATINIZATION *

D. J. KOOYMAN, PH.D.
ST. LOUIS

The process by which the normal active cells of the stratum germinativum become the hard, scaly, cornified cells of the stratum corneum involves some extremely interesting chemical changes in the cell constituents. The most apparent change is that which takes place in the protein in the formation of keratin. That the fatty constituents of the cell also undergo marked changes during keratinization is suggested when histologic studies are interpreted in the light of modern concepts concerning lipids in their relation to physiologic activity.

As was pointed out in an earlier review of skin lipids,[1] the nature of the fatty substances in a tissue may reflect in a general way its physiologic activity. Thus the lipids of an inactive tissue such as the panniculus adiposus are almost entirely made up of neutral fat, that is, simple esters of fatty acids with glycerin, while those of active tissues such as liver, kidney, lung, muscle, etc., contain relatively small amounts of fat and large amounts of phospholipids and unsaponifiable lipids. Not only are phospholipids qualitatively characteristic of active tissues, but quantitatively as well. Bloor,[2] for example, in analyses of various muscles of the ox found that the phospholipid content was roughly proportional to the activity of the muscle. The heart muscle, being the most active, had the highest phospholipid content; the diaphragm came next, then the muscles of the jaw, which in the case of a cud-chewing animal would be next in order of activity, then the neck muscles and finally and least active the muscles of the buttocks.

These findings become even more interesting in view of the work of Mayer, Rathery and Shaeffer,[3] who showed that the mitochondria

* Submitted for publication, Jan. 22, 1932.

* Studies, Observations and Reports from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., service of Drs. M. F. Engman and William H. Mook.

1. Kooyman, D. J.: Lipids of the Skin: A Review, Arch. Dermat. & Syph. **25**:245 (Feb.) 1932.

2. Bloor, W. R.: Distribution of Unsaturated Fatty Acids in Tissues: II. Voluntary Muscles of Beef, J. Biol. Chem. **72**:327, 1927.

3. Mayer, A.; Rathery, F., and Shaeffer, G.: Les granulations ou mitochondries de la cellule hépatique, J. de physiol. et de path. gén. **16**:607, 1914.

of cells are phospholipid in nature, and of Bullard,[4] who found that mitochondria were more than twice as abundant in the cells of heart muscle as in those of skeletal muscle. Cowdry [5] also pointed out that a direct relationship exists between mitochondria and protoplasmic activity.

The process of keratinization in the epidermis is an excellent example of cells undergoing a change in activity. The very active cells of the stratum germinativum which are continually multiplying contain many mitochondria. As the cells are displaced toward the skin surface and keratinization takes place, the mitochondria become fewer in number until in the completely keratinized cells of the stratum lucidum or stratum corneum they may be entirely absent. Not only mitochondria, but all cell organs apparently disappear during this process.

Histochemical studies have shown that the staining qualities of the lipids in the nonkeratinized are different from those of the keratinized layers of the epidermis. Thus, Nicolau [6] could not demonstrate particles staining with sudan III in keratinized layers, but found many in the more basal layers of the epidermis. Unna,[7] on the other hand, showed that the entire horny layer could be blackened by osmic acid, and that cholesterol esters were present in the keratinized layers, but only free cholesterol in the nonkeratinized layers.

The present investigation was undertaken with a view to determining by means of microchemical methods some of the changes that occur in the cell lipids during keratinization.

MATERIALS FOR ANALYSIS

The analyses were made exclusively of skin from the sole or the palm, because of the absence of hair and sebaceous glands on these parts. The presence and secretions of sebaceous glands, it was thought, might disturb the picture of inherent cell lipids.

Samples of completely keratinized cells of the stratum corneum were obtained by catching the grindings of the superficial layers from the palmar surfaces, a rather coarse emery wheel being used, or by paring material from the thick stratum corneum of the sole. Shavings obtained from chiropodists, collected and stored under alcohol, served very well.

When the nature of the lipids in the keratinized cells was determined, any difference in those of the unkeratinized cells could be arrived at indirectly by analysis of the entire epidermis.

---

4. Bullard, H. H.: On the Occurrence and Physiological Significance of Fat in the Muscle Fibers of the Normal Myocardium and Atrio-Ventricular System: Interstitial Granules (Mitochondria) and Phospholipids in Cardiac Muscle, Am. J. Anat. **19**:1, 1916.

5. Cowdry, E. V.: The Mitochondrial Constituents of Protoplasm, Contrib. Embryol. **8**:1, 1918.

6. Nicolau, S.: Recherches histologiques sur la graisse cutanée, Ann. de dermat. et syph. **2**:641, 1911.

7. Unna, P. G.: Histochemie der Haut, Leipzig, Franz Deuticke, 1928.

It was therefore necessary to have specimens of epidermis completely separated from the underlying dermis. Various mechanical methods were tried, such as miniature models of leather splitting machines, in which the skin was lead through rollers very near to a microtome or razor blade, designed and adjusted to split the skin at the papillary level. These proved to be unsatisfactory due to lack of uniformity in thickness of the epidermis, particularly on the sole. A chemical method was then tried which gave a satisfactory separation of dermis and epidermis.

Separation of Epidermis and Dermis.—The skin immediately on removal was dissected free from the grossly adhering subcutaneous fat with scissors and forceps and spread on a clean glass plate and scraped with a razor blade until all of the subcutaneous tissues were removed. It was then placed in a cold 1 per cent solution of acetic acid and allowed to stand in the refrigerator for from six to twenty-four hours, usually overnight. Swelling took place, and the epidermis separated in wrinkles from the dermis. For the shorter periods of treatment with acetic acid, it was often necessary to separate the two layers by blunt dissection. The accompanying illustration shows a photomicrograph of a section of epidermis removed by this method and also a section of the dermis from which it was removed. Several specimens of epidermis were prepared in this way and analyzed. In some cases material was scraped from the proximal surface of the epidermis and analyzed separately. This material would contain a high but variable percentage of stratum germinativum. Such samples are designated as "basal layers" in the table.

An explanation of the action of acetic acid in this method may be found in the work of Menschel,[8] who studied the effect of various acids and bases on the swelling of keratinized tissues. He found that acetic acid was particularly active in causing a swelling of all the cells of the skin from the soles, especially those of the malpighian layer. Using 12 per cent acetic acid, he observed some cytolysis in from five to six hours in the basal layers and after forty-eight hours the cells of this layer were completely cytolysed and peptized. The separation of the skin into its two component layers by means of 1 per cent acetic acid may also be due to cytolysis of the cells in the stratum germinativum. Microscopic sections of the separated layers, however, indicate that the basal layer of cells is the first to be attacked, and that even after twenty-four hours of exposure to this dilute acid cytolysis has not become very extensive.

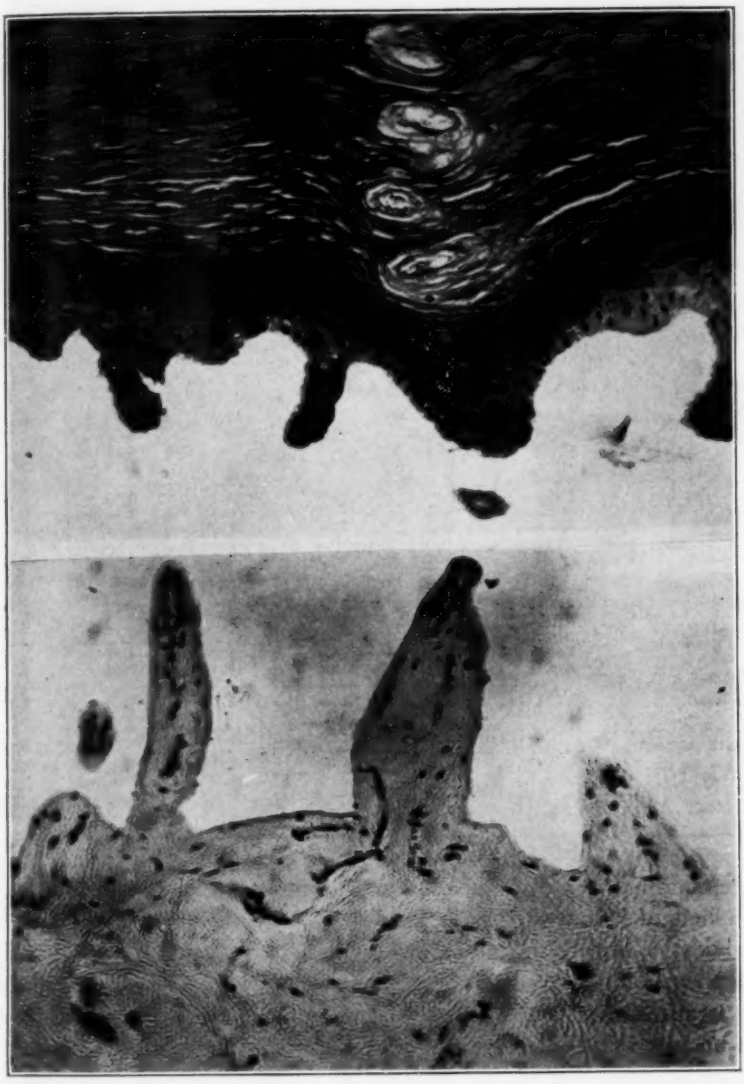
Since the lipid solvent power of this cold dilute acid is not very different from that of pure water, and since the cells remain quite intact, though very much swollen, in this treatment, it is not very probable that the cell lipids are appreciably disturbed. In order to test this, two similar pieces of skin from the same sole were analyzed, one before and the other after treating with acetic acid, and both had essentially the same lipid content.

Extraction of Lipids.—The material to be analyzed was cut up very fine with scissors, or passed through a meat chopper, placed in a fat-free extraction thimble and extracted with hot alcohol vapors in an all-glass continuous extraction apparatus for twelve hours. The alcohol was renewed after each three hour extraction period. The extracted material in the extraction thimble was then carefully dried in a vacuum desiccator and weighed, since all of the results were reported as per cent of this dry extracted weight.

The completeness of this extraction of lipid was tested by saponifying several samples of extracted material with 50 per cent sodium hydroxide (C. P.) on

8. Menschel, H.: Zur Kolloidchemie und Pharmakologie der Keratinsubstanzen der menschlichen Haut, Arch. f. exper. Path. und Pharmakol. **110**:1, 1925.

the steam bath for five hours, and extracting the acidified products of the reaction with petroleum ether. In none of the samples did this petroleum ether extract contain more than 4 per cent of the total lipids already extracted from the material.



The upper photograph shows the epidermis with the rete pegs completely separated from the dermis by the acetic acid method. The lower photograph shows the dermis with the papillae completely separated from the epidermis by the acetic acid method.

Analytic Procedures.—The combined alcoholic extracts were evaporated to dryness under diminished pressure, and the residue extracted with ethyl ether. The

ether extract was made up to volume in a volumetric flask, and aliquot parts of this extract were used for the various analyses.

The value for the phospholipid content was arrived at indirectly by determining the ether-soluble phosphorus with the micromethod of Widmark and Vahlquist,[9] and by multiplying by a theoretical factor for lecithin.

Cholesterol and cholesterol esters were determined by means of the digitonin precipitation and oxidation method devised by Okey.[10]

Bloor's [11] oxidation method was used for the determination of total fatty acids.

COMMENT

The most striking change in the lipids of the epidermal cells during keratinization occurs in the phospholipid fraction. The basal layers of

Analyses of Skin Expressed as Per Cent of Dry Extracted Skin

Material	Sample	Phospho-lipid	Cholesterol		Fatty Acids	Phospholipid / Cholesterol
			Total	Per Cent Free		
Epidermis	859-P	0.82	1.13	96.2	1.25	0.71
	860-P	0.76	0.83	91.7	1.70	0.91
	861-P	0.58	0.74	90.1	1.97	0.78
	864-P	0.50	0.93	99.3	1.99	0.53
	859-S	0.52	0.83	93.5	1.59	0.63
	860-S	0.63	0.90	88.4	1.44	0.70
	861-S	0.51	1.05	92.0	2.05	0.49
	864-S	0.69	0.79	89.8	1.74	0.87
Mean		0.63	0.90	92.6	1.71	0.70
Basal layers	864-M	4.02	1.21	97.8	4.19	3.3
	833-M	2.61	1.09	100.0	2.72	2.4
	931-M	2.45	2.04	98.0	5.05	1.2
	932-M	2.17	1.86	99.1	4.01	1.2
	933-M	1.87	1.68	96.3	3.76	1.1
Mean		2.62	1.56	98.2	3.94	1.8
Stratum corneum	6	0.11	0.59	78.6	2.78	0.19
	7	0.16	0.79	86.2	3.01	0.20
	15	0.17	0.81	81.0	2.83	0.21
Mean		0.14	0.73	81.9	2.87	0.20

the epidermis which are made up of young and active cells have a phospholipid content comparable with that of the glandular organs of the body, while the horny layers contain only traces of phospholipid. The phospholipids apparently disappear along with the cell organs during keratinization, as the cells change from a state of high activity to one of inactivity. The values found for the phospholipid content of the horny layers are of the same order of magnitude as those reported

9. Widmark, G., and Vahlquist, B.: Zur Mikrobestimmung von Calcium und Phosphor im Blute und in Geweben, Biochem. Ztschr. **230**:245, 1931.

10. Okey, Ruth: A Micro Method for the Estimation of Cholesterol by Oxidation of the Digitonide, J. Biol. Chem. **88**:376, 1930.

11. Bloor, W. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53, 1928.

by Eckstein and Wile [12] for exfoliated epidermis, which, of course, is largely keratinized material since it does not contain the malpighian layer.

Although the keratinized material was found to contain less cholesterol than the basal layers, a considerable portion of the cholesterol is retained in the cell. In many of its actions cholesterol is antagonistic to phospholipids, serving to buffer or brake their reactivity. For this reason the ratio of phospholipid to cholesterol is perhaps a more accurate index of activity than the phospholipid content alone. In spite of the fact that the basal layers of the epidermis have a higher cholesterol content than the cornified layers, the ratio of phospholipid to cholesterol is approximately ten times as great for the basal layers.

Another important change that occurs in the lipids of the epidermis during keratinization, which was long ago discovered histochemically by Unna [7] and chemically by Unna and Golodetz,[13] is the combination of cholesterol with fatty acids to form cholesterol esters. As is shown by the data in the table, practically all of the cholesterol in the basal layers is in the free or uncombined form, while in the stratum corneum approximately 18 per cent is combined with fatty acids. Using a spectrometric method for cholesterol esters, which is now obsolete, Unna and Golodetz reported that 50 per cent of the cholesterol was found to be combined in the horny layers of the epidermis. A possible explanation of the formation of the cholesterol esters is that the cholesterol combines with the fatty acids liberated by the destruction of phospholipids.

A single determination of the iodine number of the total fatty acids of the basal layers with a micromodification of the Rosenmund and Kuhnhenn [14] pyridine dibromide method gave a value of 73, while several determinations of those of stratum corneum gave values around 60. One explanation of these results is that the highly unsaturated fatty acids, characteristic of active tissues and of the stratum germinativum, are destroyed or oxidized during the evolution of the cells.

Another explanation is that the inherent fatty acids of the cells of the stratum corneum are mixed with fatty acids of low iodine number brought to the surface by sweat glands. The high fatty acid content of the stratum corneum is evidence in favor of the latter explanation, although both processes probably take place.

---

12. Eckstein, H. C., and Wile, U. J.: The Cholesterol and Phospholipid Content of the Cutaneous Epithelium of Man, J. Biol. Chem. **86**:181, 1926.

13. Unna, P. G., and Golodetz, L.: Die Hautfette, Biochem. Ztschr. **20**:469, 1909.

14. Rosenmund, K. W., and Kuhnhenn, W.: Eine neue Methode zur Jodzahlbestimmung in Fetten und Ölen unter Verwendung von Pyridinsulfatdibromide, Ztschr. f. Untersuch. d. Nahrungs und Genussmittel. **46**:154, 1923.

SUMMARY

1. A method of separating epidermis and dermis for the study of nondiffusible cell constituents is described.

2. The phospholipid content of the cells of the epidermis was found to decrease greatly during keratinization.

3. About half of the cholesterol of the epidermal cells was found to disappear during keratinization.

4. The cholesterol of the unchanged cells was found to be free, while that of the keratinized cells was found to be partly combined as cholesterol esters.

5. The ratio of phospholipid to cholesterol was found to be approximately ten times as great for the cells in the basal layers as for those in the horny layers.

6. The fatty acids of the basal layers were found to be more unsaturated than those of the horny layers.

A MICROPRECIPITATION TEST (ROSENTHAL) IN SYPHILIS *

LOUIS TULIPAN, M.D.
AND
WILLIAM DIRECTOR, M.D.
NEW YORK

In 1929, Rosenthal [1] described a rapid precipitation test for syphilis which was unlike other similar tests in that it did not require dilution of either serum or antigen. In this paper we shall describe tests performed according to Rosenthal's technic on 1,067 serums, mostly syphilitic. The method used and results obtained are as follows.

METHOD

Serum.—Sufficient blood for both the Wassermann and Rosenthal tests [2] was obtained by venipuncture, placed in separate tubes and permitted to clot; the serum was drawn off after centrifugating, and heated for thirty minutes at 56 C. in a water-bath.

Antigen.—To 5 Gm. of "Difco" beef heart powder in a test tube (6 by 1 inches [15.24 by 2.5 cm.] 20 cc. of ether was added; the tube was stoppered, allowed to stand for ten minutes, and shaken several times during the interval. This suspension was centrifugated for five minutes at moderate speed, and the resulting supernatant fluid was discarded. This process of extraction with ether was repeated three more times. The last quantity of ether used was almost colorless. The sediment that remained was left in the tube to dry. Twenty-five cubic centimeters of 95 per cent ethyl alcohol was added to the dried powder, mixed thoroughly and set aside for two days. The mixture was shaken several times daily and finally centrifugated. The supernatant fluid was decanted and kept as solution 1. It was an alcoholic, ether-insoluble, beef heart extract. Solution 2 was a 2 per cent solution of cholesterol (Merck) in acetone, which had been in the incubator at 37 C. for several hours to insure complete solution. If any precipitate appeared while the solution of cholesterol stood at room temperature, it was removed by centrifugating. Solutions 1 and 2 were used as stock solutions, and were serviceable for several months. For use in testing, 1 cc. of each solution was placed in a small test tube, where turbidity usually resulted. After an interval of ten minutes, the mixture was centrifugated

* Submitted for publication, May 21, 1931.

* From the Department of Dermatology and Syphilology, New York University Medical School, service of Dr. Howard Fox.

1. Rosenthal, L.: A Rapid Precipitation Test for Syphilis, Proc. Soc. Exper. Biol. & Med. **27**:61, 1929.

2. The serums used came from the Department of Dermatology and Syphilology, New York University. On all serums complement-fixation tests were done by the serologic laboratory of the department. Reports were received several days after the Rosenthal tests had been made and recorded.

and a clear fluid obtained. This was poured into another test tube which contained one loopful of Grubler's methylene blue powder (methylthionine chloride, U. S. P.), and was shaken until the dye had dissolved. The dye merely emphasized the clumping reaction but in no way interfered with the test. This working antigen was satisfactorily used for from two to three weeks.

Glassware.—A hollow ground glass slide and two capillary pipets were used for each test. To obtain pipets of equal size and diameter for measuring the serum

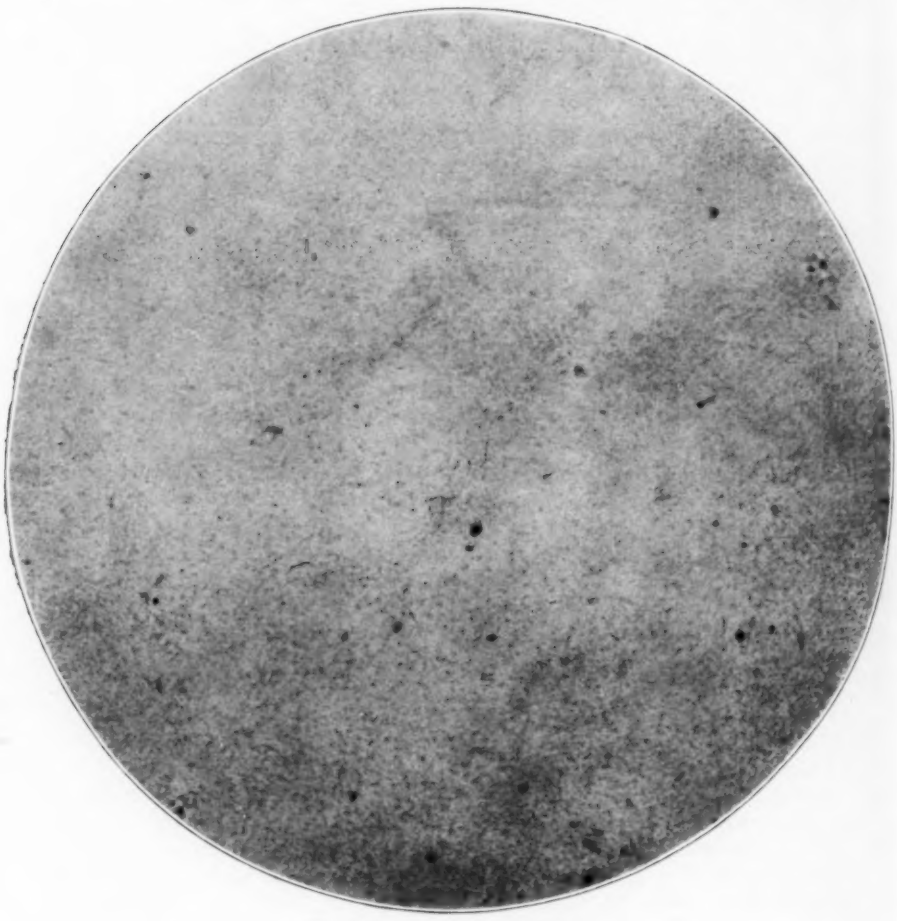


Fig. 1.—A negative reaction.

and antigen, a piece of glass tubing (10 or 12 inches [25.4 or 30.48 cm.] long and ⅛ inch [0.3 cm.] in diameter) having both ends plugged with cotton, was heated at the center in the Bunsen flame, drawn out to the proper size and separated in the middle by flaming.

Performance of the Test.—In the concavity of a hollow ground slide, 4 drops of serum were blown from the pipet, and on this 1 drop of antigen was floated. After standing at room temperature for two minutes, the two fluids were thoroughly mixed with the corner of a slide, rotated thirty times in the hollow of the slide, and read.

Reading.—The reading was done with the microscope under low power magnification (1 to 80) with the diaphragm sufficiently narrowed to give the proper illumination. Focusing on the surface of the mixture gave the best readings and made differentiation between clumping and any impurities or cholesterol crystals easy.

A negative reaction showed as a clear blue field with evenly dispersed fine granules.

A positive reaction was evidenced by clumping of the granules.

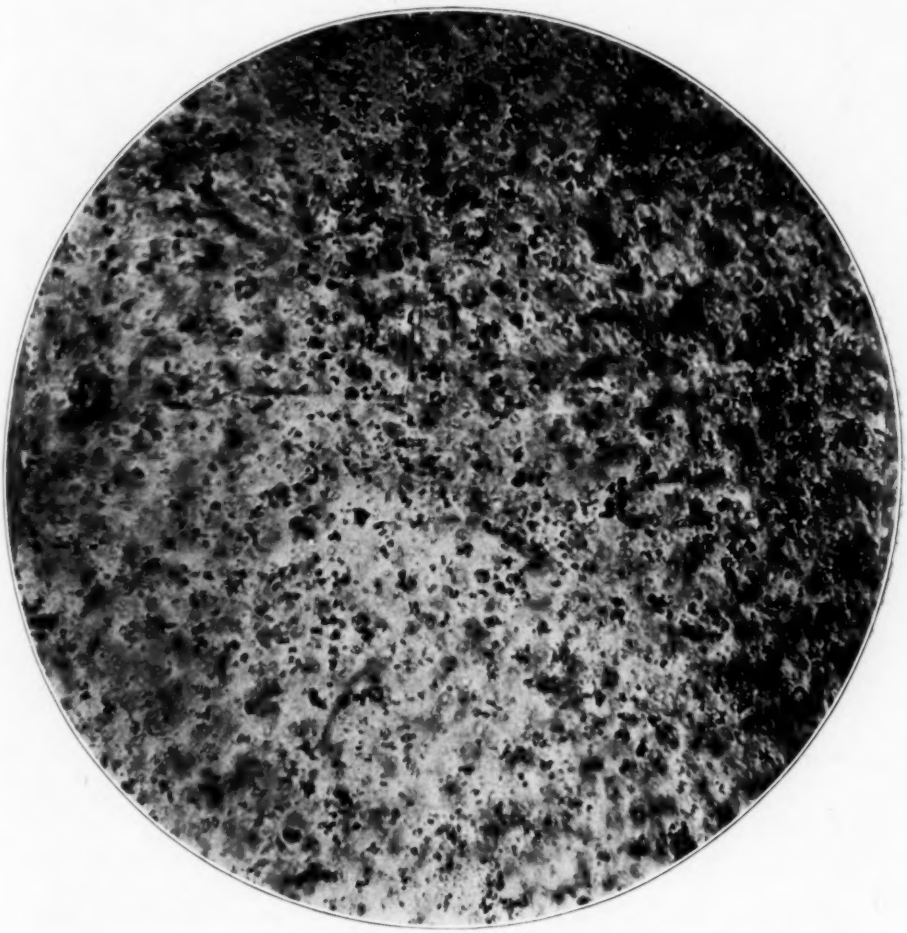


Fig. 2.—A strongly positive reaction.

1. Very large clumps, with no granules in the surrounding fluid were interpreted as strongly positive.

2. Smaller clumps than those shown in figure 1, also without granules in the surrounding fluid, were interpreted as positive.

3. The smallest well defined clumps were said to be weakly positive.

4. Small poorly defined clumps of granules, with a surrounding granular field, were interpreted as doubtful.

RESULTS

The results of the tests are given in table 1.

As a matter of definition, cases were called clinically nonsyphilitic when the history and objective signs were not those of syphilis and when serologic tests, past or present, were negative. Clinically syphilitic

TABLE 1.—*Results of Wassermann and Rosenthal Tests for Syphilis*

1. Total serums tested		1,067	
2. Serums from clinically nonsyphilitic cases		439	
(a) Wassermann and Rosenthal reactions both negative		439	
(b) Wassermann reaction negative; Rosenthal reaction positive (false positive)		0	
3. Serums from clinically syphilitic cases		628	
(a) Wassermann and Rosenthal reactions both negative	204		547
(b) Wassermann and Rosenthal reactions both positive	343		
(c) Wassermann reaction negative; Rosenthal reaction positive	64		81
(d) Wassermann reaction positive; Rosenthal reaction negative	17		

TABLE 2.—*Analysis of Rosenthal Test on 628 Syphilitic Serums*

	Agree		Disagree	
Stage of Syphilis	Wassermann and Rosenthal Both Positive	Wassermann and Rosenthal Both Negative	Wassermann Negative, Rosenthal Positive	Wassermann Positive, Rosenthal Negative
Primary				
Untreated	24	42	7	1
Treated	3	11	1	0
Secondary				
Untreated	37	9	2	0
Treated	7	19	5	1
Tertiary				
Untreated	124	15	9	4
Treated	148	92	40	11
Provocative	..	16		

cases were those with a history of previous infection, treatment or positive reactions or that showed signs of the disease.

Several comments might be made on the analysis of the cases given in table 2. No falsely positive Rosenthal reactions were found in the nonsyphilitic serums. The majority of disagreements between the Wassermann and Rosenthal tests occurred in the tertiary cases and in those in which treatment was given. In the latter cases, the Rosenthal

test gave more positive reactions than the Wassermann test, showing a tendency to remain positive under therapy longer than did the complement-fixation test. There was also some indication that the precipitation test became positive in the primary stage earlier than did the Wassermann test.

Fig. 3.—A weakly positive reaction.

COMMENT

We have no desire to advocate the substitution of the Rosenthal test for any existing test for syphilis. However, we believe that it has distinct advantages and is a valuable addition to the serologic armamentarium. No single test should be relied on in the laboratory confirmation of the clinical diagnosis of syphilis. As a check up on any other test, the Rosenthal precipitation reaction can be of great service.

The question always arises: Why should a new test be adopted when several similar ones already exist? The answer is that any procedure by which one or two steps in technic are eliminated, such as dilution of antigen or serum, duplication of tests for one serum, special preparation of slides with paraffin rings,[3] etc., is distinctly desirable. The Rosenthal test, despite its rapidity and simplicity, makes no sacrifice in accuracy.

There are occasions when a rapid test for syphilis is very advantageous. A physician need lose no time in obtaining a serologic report when a patient presents himself at his office with clinical signs of syphilis. Within an hour a report may be had, and treatment can at once be instituted. A doubtful diagnosis of syphilis may be established in either a positive or a negative direction while the patient waits in the doctor's office. One can realize the extreme importance of such aid in the case of a practitioner who is some distance away from any center for obtaining the necessary information. In hospitals, the Rosenthal test may serve as an emergency control in determining the suitability for the transfusion of the blood of a donor who has never had his blood tested or of one who has had a test at some previous time. There are also cases in which there is a question of an acute surgical condition in the abdomen or gastric crisis. Certainly in such instances, a rapid, accurate test would be of invaluable help.

SUMMARY

The Rosenthal microprecipitation test in 628 syphilitic and 439 nonsyphilitic cases agreed closely with the corresponding Wassermann tests.

3. Kline, B. S.: Simple Precipitation Test for Syphilis with Small Quantities of Defibrinated Blood, J. Lab. & Clin. Med. **14**:764 (May) 1929.

II. THE SUPERFICIAL LYMPH GLANDS IN EARLY SYPHILIS *

HENRY E. MICHELSON, M.D.
WITH THE COLLABORATION OF ELMER M. RUSTEN, M.D.
MINNEAPOLIS

In our first publication [1] on the lymphatic glands in early syphilis we reported our studies on the inguinal nodes with reference to the occurrence of a tuberculoid structure. At that time we had examined nodes from twenty-nine untreated syphilitic patients and found a tuberculoid structure in eight of the preparations examined. In the next year,[2] we continued our investigations along the same lines and increased the total number of specimens examined to fifty, which were divided as noted in the accompanying tables.

It will be noted that the percentage of glands showing tuberculoid reaction was found to be fairly constant for the three years' work.

Since our article was published, Zurhelle [3] has commented on the publication and has referred to literature [4] that had previously related the observations of giant cells in sections of lymphatic glands in early syphilis. We acknowledge this information and the splendid section on the lymphatics in syphilis in the "Handbuch." [5] This monograph has been freely consulted and contains, of course, an exhaustive bibliography. Saleeby and Greenbaum [6] recently made a comparative biologic and histologic study of lymphatic glands from syphilitic patients; among other important discoveries he reported the observation of tuberculoid

* Submitted for publication, Feb. 8, 1931.

* From the Division of Dermatology, University of Minnesota, Henry E. Michelson, director.

* This study was made under a grant from the Committee on Research in Syphilis, Incorporated.

* Read at the Fifty-Fourth Annual Meeting of the American Dermatologic Association, Toronto, Canada, June, 1931.

1. Michelson, Henry E.: The Occurrence of Tuberculoid Reactions in the Inguinal Glands in Early Syphilis, Arch. Dermat. & Syph. **19**:66 (Jan.) 1929.

2. Michelson, Henry E.: The Lymph Nodes in Early Syphilis, read before the Minnesota Pathological Society, Minneapolis, Feb. 19, 1929.

3. Zurhelle, E.: Abstr. of Michelson's paper, Zentralbl. f. Haut-u. Geschlechtskr. **30**:647 (July 5) 1929.

4. Power, D'Arcy, and Murphy, J. Keogh: A System of Syphilis, London, Oxford University Press, 1908, vol. 1, p. 157.

5. Zurhelle, E., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 17, p. 1.

6. Saleeby, Eli, and Greenbaum, Sigmund S.: Comparative Biologic and Histologic Study of Lymph Glands from Syphilitic Patients, J. A. M. A. **96**:98 (Jan. 10) 1931.

structure in three of twenty-one specimens studied. However, their material consisted of only one primary case of syphilis, and twelve secondary and eight latent cases, and they did not state in which group they encountered the tuberculoid reactions. Nevertheless, we were pleased to have these corroborative observations recorded.

MATERIAL AND PROCEDURES

We again confined our activity to the study of the glands in only primary and active syphilis. As will be noted in table 2, we examined a total of 145 glands. In each case the diagnosis was confirmed and established beyond doubt.

TABLE 1.—*Incidence of Tuberculoid Structures in Inguinal Nodes in Syphilitic Patients*

	Primary Syphilis Wassermann Reaction Negative	Primary Syphilis Wassermann Reaction Positive	Secondary Syphilis Wassermann Reaction Positive
Number of cases	7	18	25
Banal reaction	5	16	16
Tuberculoid structure	2	2	9

TABLE 2.—*Percentage of Tuberculoid Reaction of Glands Noted During Period of Three Years*

	First Year	Second Year	Third Year (Total)
Total number of cases	29	50	145
Banal reaction	21	27	104
Tuberculoid structure	8	13	41
Percentage of tuberculoid reactions	27	26	28

In the discussion of our first paper, it was suggested by Dr. Walter Highman and Professor Bruno Bloch that it would be valuable if studies with tuberculin and the luotest [7] were done in a group of cases in order to record the behavior to these agents of persons with syphilis who showed tuberculoid reaction in the inguinal nodes.

Tuberculin Reactions.—In sixty-five persons with early syphilis, intradermal tuberculin tests were given, a 1:1,000 dilution of old tuberculin being used according to the method of Mantoux. Sites of injection that showed a definite area of redness and induration in twenty-four hours were judged positive. In Minnesota, the average of positive results when the tests are done on a large scale is about 20 per cent. In our series there were fifty-one negative and fourteen positive reactions, a percentage of 22. Therefore, our material was

7. Luotest is the proprietary name for a product that Muller and Brandt of the serotherapeutic institute of Vienna have prepared. This product is an extract from the organs of animals infected with syphilis. It has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

average in this respect. Of the fourteen positive cases, the glands showed tuberculoid structure in only seven sections, or in 50 per cent. We could find no parallelism between the positive tuberculin test, as done, and the tuberculoid structure in the superficial lymphatic nodes.

THE LOUTEST

Luotest was injected intradermally in twenty-six instances, following the accepted technic of Muller and Brandt from the State Serum Institute of Vienna. We did not observe a single positive reaction. In these twenty-six cases the glands showed nine examples of tuberculoid structure. Apparently the presence of tuberculoid reaction in the lymphatics is not an indication that the individual is in such a state of allergy that he will react positively to luotest. When the skin shows the histologic characteristics of tertiary syphilis, the individual often reacts positively to luotest. If the presence of tuberculoid structure in lesions of the skin in syphilis, tuberculosis, trichophytosis and a few other conditions is a proof that the patient is allergic, one would expect that the presence of tuberculoid structure in the lymph nodes might be interpreted in the same manner. In patients with lesions of the skin that microscopically show tuberculoid structure, the luotest was frequently positive. In nine patients with syphilis in whom the superficial lymphatics showed tuberculoid structure, the luotest was negative. Either the luotest is not sensitive enough to detect early allergic reactions that are first manifested by tuberculoid structure in the lymphatics or the tuberculoid reaction is brought about in these complicated structures by another mechanism and this reaction in the glands cannot be interpreted in the same way as when it is found elsewhere. To be sure, there is a difference between the tuberculoid reactions noted by us and gummatous lymphadenitis. Löwenbach [8] stated that gummas of the lymph glands are not like ordinary gummas elsewhere, but that they histologically resemble large cell sarcomas as well as tuberculosis. In citing Löwenbach's work, however, Sternberg expressed the opinion that his case was an example of lymphogranulomatosis occurring in a syphilitic patient.

GUMMATOUS LYMPHADENITIS

Lymphadenitis of the tertiary period is not a common occurrence, and there are not enough microscopic descriptions of gummas of the lymph glands in the literature to determine the essentials for such a microscopic diagnosis. Cummer [9] reviewed the clinical aspects of this

8. Löwenbach, George: Beitrag zur Histologie der gummosen Lymphome, Arch. f. Dermat. u. Syph. **48**:74, 1899.

9. Cummer, C. L.: The Lymphadenitis of Tertiary Syphilis with Survey of the Literature, Am. J. Syph. **12**:13 (Jan.) 1928.

subject, and concluded that lymphadenitis in late syphilis was not as rare as had been supposed. The older literature is not reliable on the histology of lymphatic gummas. Buday, cited by Sternberg, stated that the picture is rather changeable, but consists of a foreign granulation tissue with central necrosis.

We had the privilege of examining two specimens of gummatous lymphadenitis. One section was from a patient seen by Dr. Winer of my staff, with Professor Oppenheim at the Wilhelminenspital in Vienna, in January, 1930. The patient had inguinal adenitis of considerable duration, without other signs of syphilis, but with a history

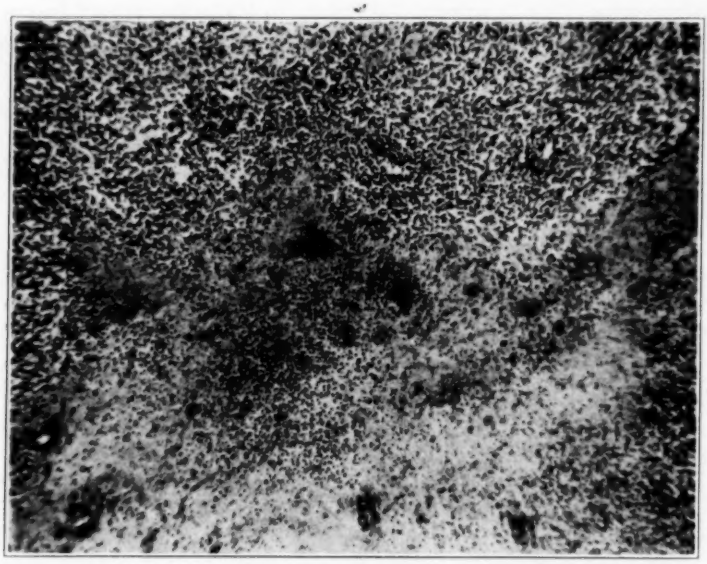


Fig. 1.—True gummatous lymphadenitis showing circumscribed necrosis.

of having had a syphilitic infection many years previously. The Wassermann reaction was positive. The section showed marked thickening of the capsule; one half of the gland was normal while in the other pole there was a sharply circumscribed area of liquefaction. In this area there were numerous isolated and clustered plasma cells, polymorphonuclear cells and tissue débris. There were no epithelioid or giant cells and no semblance to tuberculoid structure. The necrotic area was sharply demarcated, but there was no apparent effort at walling off this area.

The case from which the second specimen was taken was studied in the department of Dr. Udo J. Wile at the University Hospital in Ann Arbor, Mich.

The capsule of this gland (fig. 1) was tremendously thickened and infiltrated. The central portion of the pulp, especially about the hilus, showed greatly congested blood vessels. The greatest part of the central portion of the gland was in a state of necrosis, so that no cell outlines were seen. Within this necrotic mass there were many new blood vessels which were congested and even thrombosed. The whole appearance was that of granulation tissue. The tissue about the necrosis was fairly normal. There was no tuberculoid structure or giant cells, but there were a few epithelioid cells. We readily realized from the examintion of these two specimens that it would be difficult to differentiate between caseating tuberculosis and these gummas, but our series of glands with tuberculoid structure in early syphilis were different. We believe that the outstanding difference is that in early syphilis the entire gland seems to be reacting to a toxic influence which brings about different reactions of the tissue in different subjects, but the influence exerted is not great enough to cause necrosis.

In the gummatous glands a portion of the gland seems to be normal while the gumma proper shows a central necrosis or liquefaction that is fairly well demarcated from the rest of the gland.

EPITROCHLEAR AND CERVICAL NODES

In order to compare the histology of the inguinal nodes with that found in other superficial lymphatics frequently enlarged in early syphilis, we excised eight epitrochlear and two cervical glands from ten patients with early untreated syphilis. Five of these cases showed tuberculoid structure. We estimated that the patients had had the disease for from twelve to fourteen weeks when the glands were removed.

It will be noted that in this group of glands the percentage of positive reactions is 50, which is much higher than that found in the primary cases with negative Wassermann reactions in which the percentage was about 20, and also higher than that in the frank secondary cases, in which we encountered 28 per cent of positive reactions. It must be stated that the epitrochlear glands were removed from laborers whose hands had been subjected to repeated trauma, and this may have had some influence on the anatomic reaction of the epitrochlear glands. We shall make an effort to procure a series of epitrochlear nodes from nonsyphilitic subjects and investigate the histologic structure encountered.

SEX

In a total of twenty-three patients in whom the inguinal glands showed a tuberculoid structure, there were sixteen males and seven females. The precise anatomic location of the chancre on the genitals

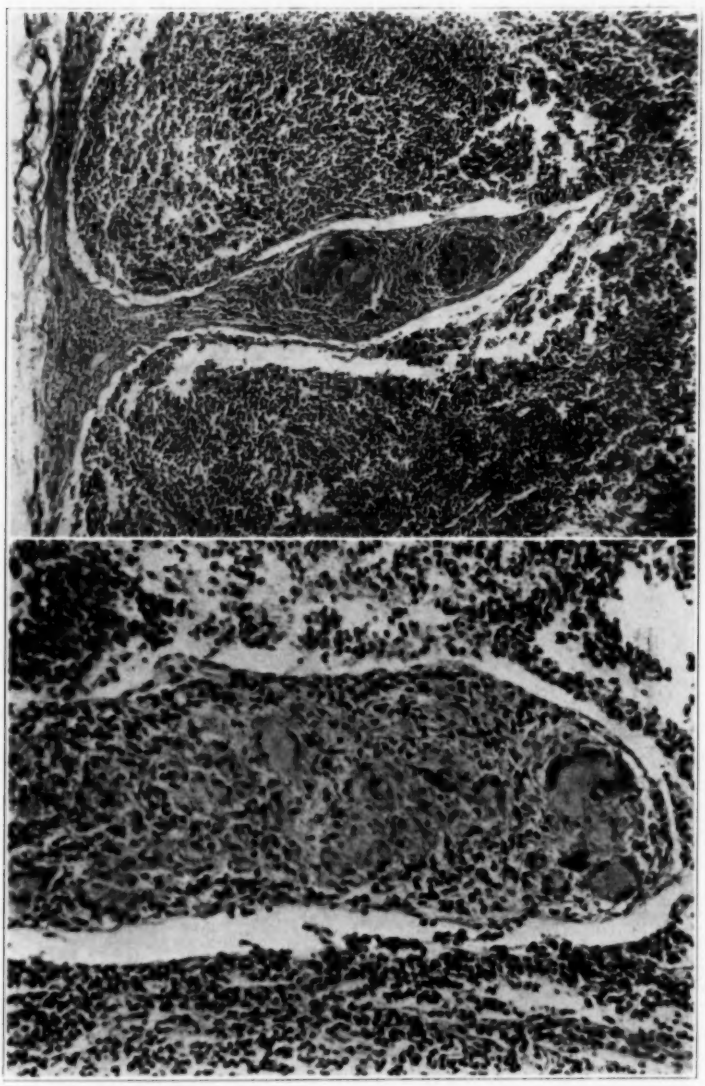


Fig. 2.—High and low power photomicrographs of marked reticular proliferation with endothelial and giant cells. Note connection with capsule.

was not recorded, but we doubt that the particular location, provided the external genitals were involved, could have been a deciding factor.

TUBERCULOID STRUCTURE

In our first publication we described two distinct types of tuberculoid structure that were found in the superficial nodes in early syphilis. We likened the one type to indurative or epithelioid tuberculosis, and the other type resembled the features found in disseminated miliary tuberculosis of the lymphatics. These two types have been frequently encountered again, but in addition we have noted several other types of reaction in which epithelioid and giant cells seemed to replace or were added to the normal lymphatic and trabecular structure.

An extraordinary type of reaction (fig. 2) was noted in the inguinal gland removed from a woman, aged 23, who stated that she had noticed a generalized eruption on her body for the past three weeks. Examination revealed a widely distributed papular eruption, general superficial adenitis, mucous patches on the fauces, leukoderma of the colon and specific alopecia. The Wassermann and Kahn tests gave positive reactions, while the luotest and the Mantoux reaction were negative. There was no other disease involving the genitals.

The section (fig. 2) was remarkable in that there was a marked involvement of the trabeculae of the gland by a tuberculoid reaction. The capsule of the gland was thinned, whereas the trabeculae were much thickened in areas, especially toward the center of the lymph pulp where they were noted as clublike projections made up almost entirely of epithelioid and giant cells. These projections maintained a connection with the capsule by a mere strand, and in certain areas this strand was lost, which left an isolated island of reticular tissue that showed a marked tuberculoid structure. We did not see this particular type of reaction often, and evidently it is an unusual pathologic change. It is probably due to the well known predilection of spirochetes for connective tissue. Klingmüller [10] cited a similar observation in leprosy.

The rest of this particular section revealed an occasional nest of epithelioid and giant cells, and here and there a single giant cell was seen lying in a mass of lymphatic cells. No areas of necrosis were noted.

Another type of reaction noted in our further study of these glands is a type that Prof. Carl Sternberg [11] has mentioned in his section on

10. Klingmüller, Victor, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 10, p. 402.

11. Sternberg, Carl: Die Lymphknote, in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, p. 256.

the lymph nodes in Henke and Lubarsch's "Handbuch." This type is the so-called epithelioid germ center and is shown in figure 3. The inguinal node shown was excised from a woman who showed a marked generalized papular eruption, condylomata lata about the genitals and mucous patches on the tonsils. The Wassermann and Kahn reactions were positive, while the Mantoux test and the luotest gave negative results.

It will be noted that in the midst of the ordinary adenoid tissue of the gland there is a nest of epithelioid cells which are closely packed and have the tendency to be concentrically arranged, giving a whorl-like

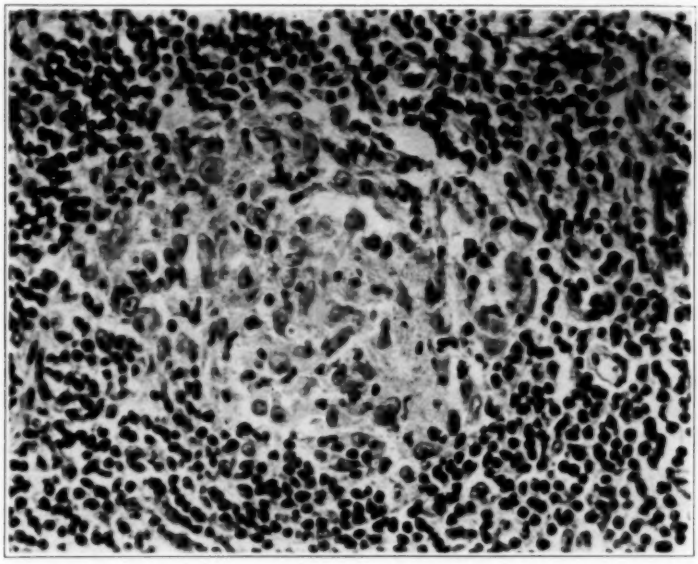


Fig. 3.—Epithelial germ center. Note whorl-like arrangement of epithelioid cells.

appearance. A few lymphocytes with pale-staining nuclei are incorporated in this mass of epithelioid cells. These cells are about the type one would expect to find in a germ center. There are no multinucleated cells in this area. Sternberg cited the work of Heineke, who showed that under the influence of injurious substances cells that are similar to lymphoblasts but that have a different source of origin and a different function to perform may develop in the germ center. Under the effect of the roentgen rays, the lymph nodes in microscopic sections from the guinea-pig and rabbit showed that in the follicles the lymphocytes were replaced by epithelioid cells concentrically arranged, giving the appearance of a cut onion. Under ordinary conditions epithelioid cells are not found in the germ centers. Waetjen also demonstrated that in acute

degeneration of the lymph nodes brought about by intravenous or subcutaneous injections of arsenic, the proliferation of the supportive structures is proportionate to the degenerative changes of the lymphatic tissue and that when there is a completely developed epithelioid change in the germ center, lymphocytes are no longer formed there. Sternberg also cited other researches that have shown that phagocytosis is found only in the reticulo-endothelium and not in the lymphocytes.

Evidently stimulation of the reticulo-endothelium in the lymph nodes is brought about by the invading spirochetes, and possibly the degree of proliferation is dependent on well known factors such as the age of infection, the resistance of the host and the virulence of the invader. Unfortunately, we were unable from our observations to draw any conclusions that would shed light on the degree of immunity present when tuberculoid structures were encountered in the glands.

Stoeckenius [12] studied four cases of newly acquired syphilis that came to autopsy from other causes. From his studies of the cytology found in various lymph nodes he stated that various types of cells are encountered, many of lymphatic origin, but also a great number that are the result of proliferation of the reticulo-endothelium. He mentioned in particular giant cells of various types, many of which resembled Langhans' giant cells. Stoeckenius also remarked that he did not encounter caseation, a fact that Dr. E. T. Bell [13] has often discussed when examining our material. Our pathologists, who have examined a large number of these glands from patients with early syphilis, agreed that the microscopic changes are not pathognomonic in either the banal or the tuberculoid type of reaction. There seems to be a certain chronological sequence of changes, but they are not definite, and in no way may they be compared with the clinical course of events. We are desirous of obtaining a series of inguinal glands from persons in whom there is a regional glandular enlargement but in whom syphilis has been entirely eliminated as a factor in the enlargement. We removed one gland (fig. 4) from a woman, aged 27, who had a nonsyphilitic vaginal discharge, without anatomic lesions. She had noticed enlargement of the inguinal glands for three weeks. There were no clinical or serologic evidences of syphilis, and such symptoms did not develop during the long period of observation. The Wassermann and Kahn reactions, as well as the reaction to the Mantoux test, remained negative.

Microscopically, the gland showed marked reticulo-endothelial proliferation without the formation of giant cells, but it so resembled cer-

12. Stoeckenius, W.: Beobachtungen an Todesfallen bei frischer Syphilis, Beitr. z. path. Anat. u. z. allg. Path. **68**:135, 1921.

13. Bell, E. T.: Personal communication to the authors. (Professor Bell is professor of pathology at the University of Minnesota.)

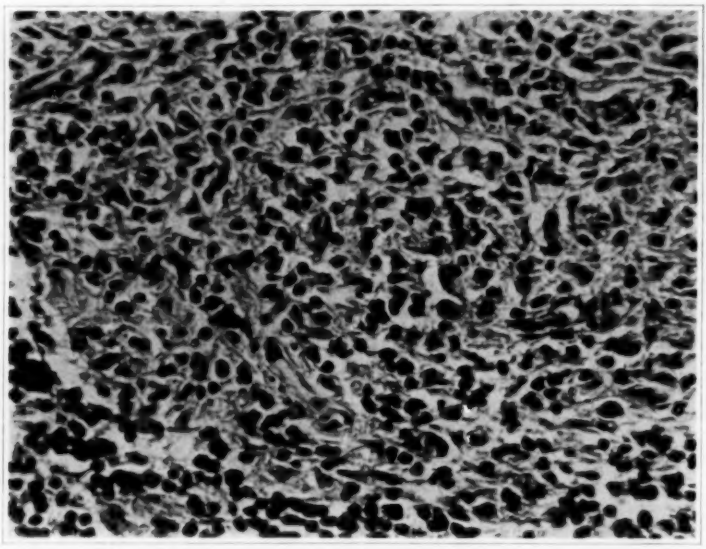


Fig. 4.—Marked, diffuse proliferation of connective tissue in a nonsyphilitic gland.

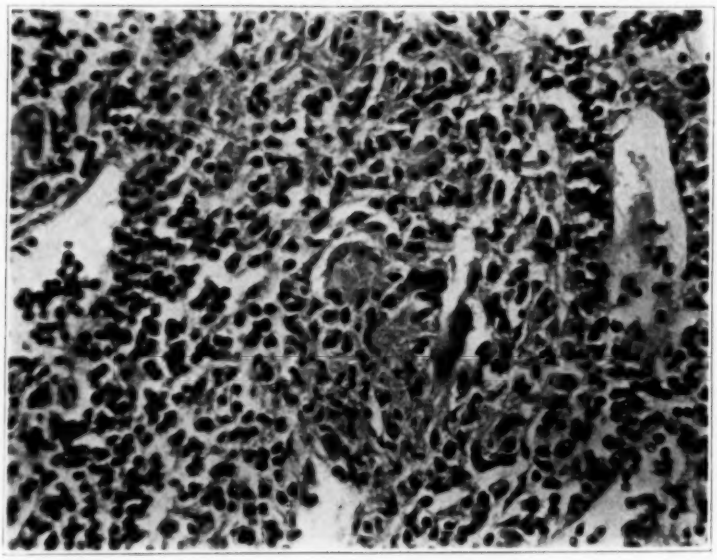


Fig. 5.—Isolated giant cell resembling a thrombosed vessel.

tain sections of glands known to be syphilitic that we were thoroughly convinced that regardless of the microscopic observations, one must know the clinical facts and should attempt to draw conclusions only when these were known.

In many of our sections (fig. 5) we noted isolated multinucleated cells which on first view had the appearance of a thrombosed blood vessel, but continued search in the section often revealed other similar cells surrounded by epithelioid cells (fig. 6). Such was the case in the gland removed from a woman, aged 28, who had a generalized papular eruption, mucous patches on the tonsils and generalized

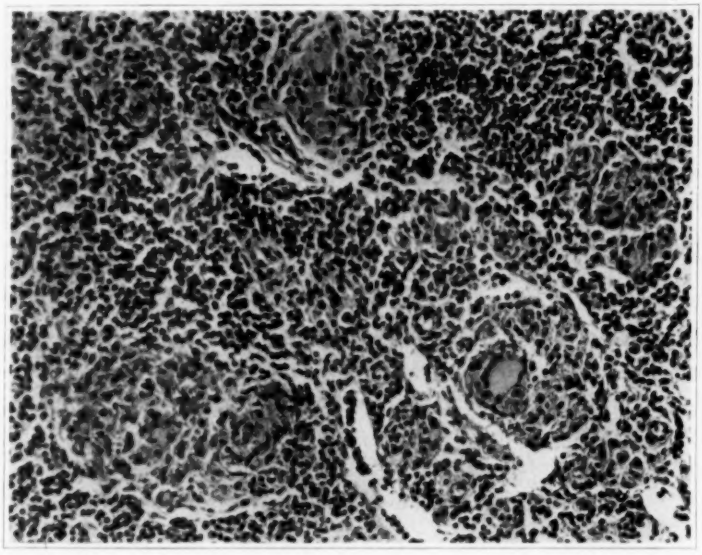


Fig. 6.—Marked tuberculoid structure showing epithelioid germ centers and giant cells.

adenopathy. The Wassermann and Kahn reactions were positive, while the luotest gave negative results. In this case there were numerous epithelioid centers with large multinucleated cells enclosed. This type of reaction seems to be at the expense of the lymphoid tissue. The capsule of the gland was much reduced in thickness, and there were few trabeculae left. In certain syphilitic glands the reaction to the infection seemed to diminish the amount of reticular tissue, while in others the chief reaction centers seemed to be in this tissue.

SUMMARY

Our studies on the superficial glands in early syphilis have been of extreme interest in that we were unable to show by any known tests

that the presence of a tuberculoid structure was an indication of an allergic state. In this respect tuberculoid reactions in the skin in syphilis and in lymphatic tissue are apparently brought about by different mechanisms.

Furthermore, we believe that the tuberculoid reaction as encountered in early syphilis cannot be looked on as an early tertiarism or gummatous change because of the complete absence of necrosis in the early tuberculoid glands as compared with the late true gummatous change. Apparently there is a gradual transition from early tuberculoid reaction to a type of tissue change that tends to resemble true gummas, but a gland in which tuberculoid structure and real gumma are shown in the same section has not been found.

From the work cited it may be concluded that lymph nodes may react against an invader or noxious substance by a local proliferation of the reticulo-endothelial system, and probably that proliferation takes place in the glands that show tuberculoid structure. It has not been determined why certain persons react in this manner and others in the same stage of the disease show only a subacute inflammatory change in the superficial lymphatics.

We believe that continued studies along this line will be valuable and may throw some light on immunity in syphilis.

The skin and the superficial lymphatics are easily studied microscopically, and our observations show that these two tissues react differently when invaded by the spirochetes of syphilis. Perhaps studies on other tissues in early syphilis would also show the extreme variability in the reaction of certain tissues against invasion by the spirochete, and perhaps a tissue may develop immunity or susceptibility according to its own peculiarities.

CONCLUSIONS

1. One hundred and forty-five lymph nodes excised from patients with early untreated syphilis were examined.

2. In approximately 27 per cent of the specimens, tuberculoid structure was present.

3. The test with tuberculin, performed on fourteen patients whose glands showed tuberculoid structure, was positive seven times.

4. The luotest was negative when performed on nine patients whose glands showed tuberculoid structure.

5. Tuberculoid reactions found in the lymphatics in early syphilis are variable in type, and apparently the state of allergy is not the same as when this reaction is found in the skin.

6. True gummas of the lymph nodes differ from the tuberculoid structure found in the nodes in early syphilis.

ABSTRACT OF DISCUSSION

DR. J. FRANK FRASER, New York: Some of these pictures look so much like the histologic picture one finds in cases of tuberculosis that this condition should have been excluded by inoculations into animals. Tuberculous lymph nodes are frequently found in persons who have died from various causes, and it is possible that they might be found in cases of syphilis.

DR. KARL G. ZWICK, Cincinnati: In view of the possibility that a previous infection with tuberculosis may influence the histologic changes resulting from a subsequent spirochetal invasion, I refer to Naegeli's report, from Aschoff's pathologic institute in Freiburg, in which he stated that 96 per cent of all persons coming to necropsy after puberty were found to have been infected at one time with the bacillus of Koch. Marfan's figures from a hospital in Paris (1923) were even higher and closely approached the statistics of the late Dr. Warthin of Ann Arbor with reference to syphilitic infections discovered at necropsy.

DR. HENRY E. MICHELSON, Minneapolis: Almost every one who has examined these slides has brought up the point that Dr. Fraser mentioned. Dr. Sweitzer has examined every one of the patients, and in only those cases in which syphilis was undoubtedly present did we make the excision. Tuberculosis of the inguinal glands is extremely rare. Usually when an inguinal node is removed from the groin of a patient who has syphilis and the patient is given antisyphilitic treatment and there is immediate response with the disappearance of the adenitis in both groins, it is a fair clinical presumption that the condition is entirely syphilitic. Sections stained for tubercle bacilli have been negative, as was to be expected. We have not made inoculations into animals, but we intend to make culture tests for tubercle bacilli in the near future.

ECONOMIC ASPECTS OF THE MANAGEMENT OF SYPHILIS*

ALBERT KEIDEL, M.D.
BALTIMORE

Conjectural estimates of the prevalence of venereal disease in the United States bid fair shortly to be replaced by more accurate information on the basis of surveys conducted by the United States Public Health Service jointly with the American Social Hygiene Association. The results obtained from a survey of twenty-five communities with a population of almost 25,000,000 have just been summarized by Usilton.[1] She arrives at the appalling conclusion that there are each year in this country 423,000 fresh infections with syphilis, the annual rate of attack being 3.46 per thousand of the population. If this figure is applied to the census reports of the numbers of the population of different age groups, it is easy to estimate that well over 10 per cent of the adults of the country are, or have at one time been, infected with syphilis.

Of the various methods for the control of syphilis available to the physician, only one is of great practical importance, that is, adequate treatment of the infectious patient. Prophylaxis, education, repression of prostitution and other methods of social hygiene all play, or can be made to play, a valuable rôle in diminishing the incidence of fresh infections; but for the physician, the important thing is treatment. If it were possible promptly to arrive at a diagnosis in all patients with infectious syphilis, and immediately to institute treatment destroying the organisms in infectious lesions, with reasonable assurance against relapse, syphilis would become an almost negligible factor in public health. The knowledge of how to accomplish this feat and the weapons with which to do it are already at hand; obviously, however, they are not being successfully applied. I believe that one of the chief reasons for failure is the high cost of the medical care, and that the element of cost prevents not only the proper treatment of many patients, but even the recognition of the syphilitic condition.

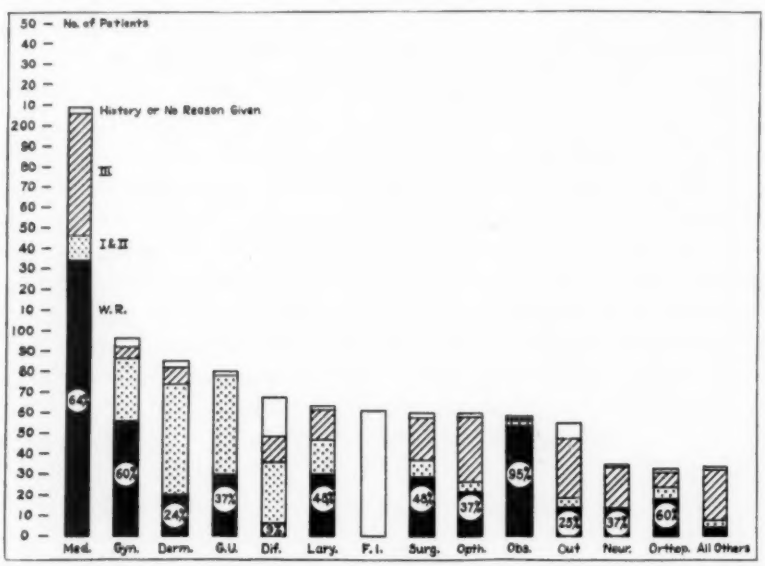
The question at once arises, What constitutes infectiousness in syphilis? It is as yet unanswerable. Early syphilis (primary, secondary or relapsing), of course; but is the patient with latent or late syphilis a carrier who may transmit the infection to others? At times he certainly is, as is witnessed by numerous tragic family stories. What of the pregnant woman with no lesions but a positive Wassermann reac-

* Submitted for publication, Feb. 8, 1931.
* Read at the Fifty-Fourth Annual Meeting of the American Dermatological Association, Toronto, Canada, June, 1931.

1. Usilton, Lida J.: Ven. Dis. Inform. **11**:543, 1930.

tion of the blood? She may not be infectious for her sexual partner, but she is certainly so for her child in utero. From the practical standpoint, the syphilologist can, I believe, take only one position; namely, that while early syphilis is surely infectious, latent and late syphilis are at least potentially so, and that control of the disease will not be accomplished until all such patients are recognized as syphilitic and brought under treatment.

Aside from the obviously impossible step of educating all practicing physicians to the point of diagnostic expertness equivalent to that of the syphilologist, how is syphilis to be recognized? It occurred to me that the average large dispensary service might serve as a cross-section of the general practice of medicine in illustrating the complaints that brought



Analysis of 1,000 consecutive admissions to the syphilic clinic at the Johns Hopkins Hospital Dispensary from the standpoint of the referring clinic and the diagnostic data actuating the transfer. *Dif.* means differentiator; *F.I.*, family investigations *Out*, sources outside the Johns Hopkins Hospital. The areas indicate the following: white area, history of syphilis; diagonal lines, late syphilis; dotted area, early syphilis; solid black area, positive Wassermann reaction only.

the patient to a physician, and the basis on which a diagnosis of syphilis was made. Accordingly, I have surveyed the last 1,000 consecutive admissions to the syphilis clinic of the Johns Hopkins Hospital, from the standpoint of the referring clinic, and the reason which that clinic had for transferring the patient to the syphilis clinic. The data are shown in the chart. Slightly more than one fifth of the patients entered the hospital with a complaint that indicated the desirability of a general medical examination. Among these 209 medical cases, the diagnosis of

syphilis was made in 134, or 64 per cent, only by virtue of the fact that a routine Wassermann test of the blood was done. The obstetric department accounted for 59 of 1,000 cases; in 55 of these 59 women, or 95 per cent, a positive Wassermann reaction was the only evidence of syphilis. The other referring clinics do not use the Wassermann test as a routine; when syphilis is diagnosed, it is usually on the basis of a definite history, or unmistakable lesions. Even so, among the 664 patients sent to the syphilis clinic from all sources other than the medical or obstetric clinics, no less than 35 per cent would have gone unrecognized as syphilitic except for the Wassermann test of the blood. These sources, of course, include in their material 22 per cent of the cases of early syphilis in which the diagnosis can usually be made without the aid of the Wassermann test. If one limits the discussion to late syphilis, Turner's [2] figures from the syphilis clinic of Johns Hopkins Hospital show that among 6,420 patients with late syphilis, the diagnosis was latent syphilis, made solely because of a positive Wassermann test of the blood in 53 per cent.

It is unnecessary to consider these figures further. They tell a story that the syphilologist has been stressing for years; namely, that thousands of cases of syphilis are unrecognized and untreated because of the failure of physicians to perform the Wassermann test more frequently as a routine. This is true even of large hospital services, such as that at Johns Hopkins, where the only outpatient clinics employing the test as a routine are the medical, obstetric and, recently, dermatologic. Some years ago, with a smaller dispensary clientele than at present, Moore and I [3] estimated that approximately 3,000 patients per year were passing through the outpatient department of Johns Hopkins with unrecognized syphilis. In private medical practice, the Wassermann test is applied as a routine by only a few internists. Failure to employ it more widely is due partly to an entangling of medical and moral ideas, partly to the obvious fact that many contacts between patient and physician are for minor reasons which do not call for a general examination, and partly because of the expense entailed. The question of cost is, I believe, of paramount importance.

COST OF LABORATORY TESTS

The practicing physician may send specimens for the Wassermann test either to a city, county or state health department, or to a private laboratory. If the former, the cost to the patient is nothing, unless,

2. Turner, T. B.: The Race and Sex Distribution of the Lesions of Syphilis in 10,000 Cases, Bull. Johns Hopkins Hosp. **46**:159, 1930.

3. Keidel, A., and Moore, J. E.: The Wassermann Reaction in the Johns Hopkins Hospital, Bull. Johns Hopkins Hosp. **34**:16, 1923.

as is too often the case, the physician makes a charge which he retains; if the latter, the cost is usually $5. There is much to be said, from the standpoint of public health, not only for free Wassermann service, but for absolutely free treatment for all patients with venereal disease—a procedure already adopted in Denmark and England. In this country, such an extension of the idea of state medicine would call forth violent protest from the medical profession and is, moreover, unlikely with our system of state and local government. Unless the public health authorities are prepared to take over the whole question of the control of venereal disease, however, there seems to be as much cause for protest against free Wassermann service for private patients, able to pay a fee, as against free urinalyses, chemical examinations of the blood or roentgen examinations. A patient who can afford to pay for a Wassermann test should pay for it.

How much should he pay? The charge of $5 persists, partly through long established custom, partly through the multiplication of small laboratories, each doing only a few tests, and thus keeping the cost artifically high because of proportionately high overhead expense. The actual cost of doing a quantitatively titered Wassermann test of the blood, with an additional flocculation test, in a small but efficient laboratory doing 200 tests per month, is $1.63 apiece. If 500 tests per month were run, the estimated cost would be 66 cents. The serologic laboratory at the Johns Hopkins Hospital, doing over 50,000 tests per year, does them at an average total cost of 29 cents each. Obviously, the prevailing fees for Wassermann tests are too high. The solution lies in a reduction of the small laboratories doing a few tests, and the centralization of this work in several larger laboratories in big cities, where the saving represented by the volume of work done can be passed on to the patient.

COST OF TREATMENT FOR SYPHILIS

Bringing down the cost of diagnostic laboratory procedures is the simplest element of the problem of control of syphilis. There remains the much more complex question of the cost of treatment. How largely this looms in the mind of the average syphilitic patient can only be appreciated by one who is in constant contact with both private and so-called charity clinic patients.

What does it cost to be treated for syphilis? Generally speaking, the average patient in this country has two available alternatives. He may go to a large clinic, where he can be treated free if his circumstances warrant it, but where he is usually called on to pay something toward the cost of his care, or he can seek private medical attention. The actual cost of treating a patient at the Johns Hopkins Hospital amounts to $1.03 per visit, including the cost of special drugs and of

all necessary laboratory procedures. A patient with early syphilis must make an average total of seventy-six visits, over a period of twenty-seven months. This brings the cost to $78, a not inconsiderable sum for the class of patients under discussion, and a staggering impossibility if two or more members of the family group must be treated, as is frequently the case.

In private practice, the cheapest available medical service in Baltimore could provide this same service for $305, if all Wassermann tests necessary for diagnosis and treatment were performed free of charge in the laboratory of the health department. Practically all of this expense would fall within the first fifteen months. This assumes that the original examination is charged at $10, each injection of an arsphenamine product at $5 and each injection of mercury or bismuth at $2.50. Incidentally, experience leads me to believe that few physicians are willing to treat patients for fees as low as this. If Wassermann tests must be charged also, the total minimum cost rises from $305 to $380. Little experience in medical economics is necessary to realize that this sort of fee schedule is possible only for the physician who treats a great many syphilitic patients, thus reducing his overhead cost, or for the physician who, treating only a few patients, does it badly.

These are the minimum fees of private practice. The average fees for the same amount of treatment on the basis of Baltimore standards might fairly be put at $650, again almost all concentrated in a period of fifteen months. The prevailing fee schedule in this instance is $10 for an injection of an arsphenamine and $5 for one of bismuth or mercury, with other fees in proportion.

The amount of treatment considered here is that for an uncomplicated case of early syphilis. If there are any complications from treatment, if the spinal fluid is discovered to be positive, if more than one patient in the family is to be treated, the cost mounts with what seems to the frightened patient to be almost geometrical progression. Moreover, only one third of the new patients in general medical practice each year have early syphilis (Usilton [1]); two-thirds have late syphilis. Here the total average duration of treatment rises from fifteen to twenty-four months or more, and the total cost from a minimum of $305 or an average of $650, to $480 or $1,050.

These sums begin to mount up to figures that are difficult even for patients in the upper level of wage earners. If the problem is one of neurosyphilis, with perhaps hospitalization, fever or intraspinal therapy, ophthalmologic consultations, etc., it is little wonder that the average patient in moderate circumstances is consumed by a panicky fear of his inability to carry out what is demanded of him. Nothing need be said of average, high or maximum fees. Patients able to afford $2,000 or $3,000 a year for medical care present no economic problem.

To what extent do these two types of medical service, clinic and private, meet the public demand for medical attention for syphilis? To what extent does their failure to meet the demand, if present, influence the incidence of fresh syphilitic infections, or cause further economic loss to the individual, the family or the community, by virtue of the fact that the patient abandons treatment when his money runs out, and subsequently breaks down because of his disease? These are largely unanswerable questions, at least in any accurate fashion. Eighty-seven per cent of the persons of both sexes gainfully employed in the United States in 1918 received incomes under $2,000 per year.[4] Taking the country as a whole, 66 per cent of the patients with venereal disease are being treated (1925-1930) at the hands of private physicians and 33 per cent in clinics. Obviously, the 66 per cent under private care do not all belong to the 13 per cent of the population earning more than $2,000 per year. Equally obviously, many such patients are either incurring a financial obligation they cannot meet, or they are taking treatment as far as their means permit, and then abandoning it regardless of whether they are "cured" or even noninfectious. The latter course is the disastrous one from the standpoint of public health. That it frequently happens is only too clear to one with a large syphilologic experience. Many patients are dismissed by their physicians while still hopelessly inadequately treated, because they are no longer able to pay their bills. Many others stop treatment voluntarily for the same reason. Some of them with more intelligence than pride come to a free clinic to complete their treatment. More of them, especially those of the "white collar" class, unfortunately do not, sometimes because of the shame of receiving charity, sometimes because unable to lose time from work to attend clinics at inconvenient hours, sometimes because of the publicity involved and sometimes because of reluctance to mingle with lower caste white patients or with Negroes.

It seems apparent from these considerations that to an even greater extent than in other forms of medical care, the main problem lies, not with the poor man who can be treated at cost or even free, nor with the well-to-do, to whom the expenditure of money for expert care is no object, but with the middle class, the great bulk of the population. Current medical literature attests the interest which the cost of medical care has for the general public and the medical profession; and the formation of a committee of distinguished physicians and laymen to consider this question speaks for the prevalent desire to do something constructive about it.

From the special standpoint of the management of the syphilitic patient, there are several steps that physicians can properly take. For

4. Bigelow, G. H.: Why the Pay Clinic, Hosp. Soc. Serv. **8**:1, 1923.

many years dermatologists, notably Stokes, have been ceaselessly advocating the simplification of methods of treatment. This does not necessarily mean a search for new and more potent spirocheticidal drugs, which can properly be left in the hands of the experimental chemotherapist, but rather the elaboration of simpler methods of treatment with the drugs already at hand. For example, many dermatologists have repeatedly stressed the superiority of arsphenamine to neoarsphenamine, and have devoted much time to a consideration of results of treatment with arsphenamine to prove this point. They have perhaps lost sight of the fact that the relatively complex technic of administration of arsphenamine weighs more heavily with the average practitioner than its reputed therapeutic superiority, and that he insists on using the simpler neoarsphenamine, even though no such accurate data as to its efficiency are available. From the practical standpoint, the time spent in eulogizing arsphenamine, which the practitioner will not use, might be more profitably employed in studying the results obtainable from neoarsphenamine, which he will use, and in elaborating a method of treatment with the simpler drug which will produce results comparable to those obtainable with the more complex. As clinicians dealing with large numbers of syphilitic patients, this would seem distinctly the task of the dermatologist.

The physician who undertakes the treatment of patients with syphilis must discuss the financial problem with his patient from several angles. He must adapt methods of treatment to his patient's financial ability to carry them out. The administration of iodides by the intravenous route may, in some instances, be slightly more advantageous than to give them by mouth, but the one means an outlay of $3 or $4 to the pharmacist for the drug, and the other the payment of $50 or $100 to the intravenous therapeutist for an equivalent amount of drug. Is the gain to the patient from the more complex method worth what it costs? The intramuscular or intravenous administration of soluble mercurial salts has a distinct place in therapy; but the physician must conscientiously decide whether thirty or forty such injections, which must be given at frequent intervals, will really be worth more to the patient's health than eight or ten intramuscular injections of an insoluble salt or a course of inunctions.

The physician who starts the treatment of a syphilitic patient has a moral and public health responsibility to see the case through to a finish. The first conversation with the patient, after the diagnosis has been established, should include a frank discussion of what treatment will probably be necessary, barring complications, and of its probable cost. In some cases, it has worked satisfactorily to do away with a set fee schedule for special procedures of treatment and, instead, to

outline probable total minimum and maximum costs, and from this to work out a monthly average fee. In this case a patient may be told, not that injections of arsphenamine will be $5, $10 or $15 apiece, but that his treatment and subsequent follow up, over a period of two and one-half years, will cost an average of $15, $25 or $35 per month, for example. If the patient, on hearing what is necessary, finds himself unable to meet the fees demanded, the physician responsible for the diagnosis is under an absolute obligation to make other arrangements for him to be properly treated either by revising his own schedule of fees downward or by referring him to a less expensive practitioner or to a clinic. It is indefensible to treat the patient until his funds are exhausted and then drop him.

The expense of carrying on the private practice of medicine is, however, sufficiently great and there is a definite point past which the physician cannot be expected to go. With the best intentions in the world on his part to keep his fees as low as is consistent with his expenses, and to extend credit whenever necessary, he is often unable to provide the long term care and the relatively costly drugs which the syphilitic person in moderate circumstances must have. There are many cultured and educated people who are unable to finance adequate medical care, and who refuse to be the recipients of charity, either from private or from state agencies. Under existing circumstances, the majority of them go without treatment, are self-treated or resort to quackery.

THE PAY CLINIC

The obvious method of bringing together the physician who wants to provide adequate medical care and the patient in moderate circumstances who wants to receive it is the pay clinic. Such an institution can furnish expert medical service and, if its volume of work is sufficiently high, can even operate at a substantial profit on fees that are impossibly low for the individual practitioner. This point is amply proved by a famous example in one of our large cities, which undertakes the management of venereal disease in general. Here treatment for early syphilis, identical with that given at the Johns Hopkins Hospital, can be furnished at a total cost of $155. This is as compared with a cost of $78 in the charity clinic at Johns Hopkins or a minimum cost of $305 to a private patient. That the public seems to appreciate the service provided is amply illustrated by the fact that at this particular pay clinic about 20,000 new patients per year are received. It is estimated that 75 per cent of these patients have annual incomes of less than $2,000, and it is highly probable that few patients actually able to pay the prevailing fees of private practice attend the clinic.

To operate successfully, the pay clinic, in addition to furnishing competent medical care, must be available to patients at hours that conflict least with the necessity for earning a living; it must furnish privacy for the patient to a degree impossible in the charity clinic, and it must be able to attract its clientele. The classification of syphilis as a venereal disease and the fact that it is associated in lay and medical minds alike with the sexual act make it impossible for a pay clinic for syphilis or for venereal disease in general to attract patients as can similar institutions with more general medical aims. The satisfied syphilitic patient does not often tell his syphilitic friends that he is pleased with his treatment and advise them to go to the same place; indeed, he is unlikely to know which of his friends has syphilis. The only ways in which the average syphilitic patient in moderate circumstances can be made aware that a pay clinic for his treatment exists are through being informed by the physician who makes the diagnosis or through advertising sponsored by the clinic.

It is generally felt throughout the medical profession that advertising by posters or in the lay press, as heretofore conducted, has been objectionable. Perhaps some way that will have the cooperation of physicians can be found to resolve the difficulty. It has been suggested that simple announcements might be utilized, stating, for example, that persons suspecting that they may have syphilis (or venereal disease) should be examined and treated if necessary, and that the available agencies for treatment in a given community be listed, beginning with "your private physician, or if you cannot afford private medical care, the following institutions," these institutions, free, part-pay and pay, being named in alphabetical order, with their addresses and hours of availability.

Other elements of antagonism of practicing physicians toward the idea of the pay clinic might also be eliminated. The type of pay clinic suggested should be sponsored by the medical profession itself rather than by lay philanthropists. It should meticulously limit its activities to patients falling within the appropriate income class, rejecting those able to finance adequate private medical care. It should scrupulously avoid intrusion into other fields of medical practice. Its professional activities should be directed by experts, and positions on its staff should be open to competent and reputable physicians, who might profitably regard a few years of association with it as post-graduate education. Finally, the members of the staff should be adequately compensated for their services.

The pay clinic seems so adequate a solution to the problem of the management of syphilis for patients in moderate circumstances that it is desirable for the medical profession, and especially for syphilologists,

to consider it carefully. If the idea of the pay clinic does not meet with approval, it is the duty of the medical profession to offer a satisfactory alternative. If none is offered, pay clinics are likely to be the outcome, or perhaps even less agreeable solutions sponsored from outside the ranks of the medical profession.

SUMMARY

The cost of the diagnosis and treatment of syphilis is a major factor in our inadequate control of the infection. The Wassermann test often is not employed in diagnosis because it costs $5, whereas it can be done accurately for as little as 29 cents. In most American cities, treatment facilities for syphilis are available only in free or part-pay clinics, at a representative one of which the cost of the treatment for early syphilis is $78; or in private practice, in which the estimated minimum cost of equivalent treatment is $305. The average cost of private treatment for the same type of patient is more than $600. Many patients of the moderate income class are inadequately treated because they cannot afford to complete the necessary treatment in private hands, and will not accept the alternative of free or part-pay clinics.

Suggested steps in the solution of this problem are: (1) simplification of existing methods of treatment; (2) the choice of the simpler and less expensive method of treatment, provided this does not entail a sacrifice of therapeutic efficiency; (3) the realization by the physician who undertakes the treatment of a syphilitic patient that he must see that treatment through to completion by one or another means; (4) the establishment of pay clinics in centers with a large population.

Certain of the prevailing objections to the pay clinic are briefly mentioned, and remedies are suggested.

ABSTRACT OF DISCUSSION

DR. HAROLD N. COLE, Cleveland: Syphilis is a public health problem. It is different from some of the problems the medical man has to take care of. The sooner the medical profession realizes this fact, the better it will be for all concerned. Other countries have already come to this decision. In Denmark they treat syphilis as a public health problem, and in England likewise. It is a question whether we are going to do that in the United States and Canada, or whether the physicians are going to take it into their own hands and do something for the benefit of the public. As Dr. Keidel very well put it, there is one lay institution in this country that is taking care of syphilis, and is doing it very well, far better than the regular family physician would do it. I might say that the Academy of Medicine in Cleveland is seriously considering right now whether it would not be a good plan for the Academy to establish a pay clinic for the treatment of patients with venereal diseases. It would be far better for the physicians to do this than to have some scalawag come in and do it for them. They could make a fair profit and be performing a real public health service, and at the same time be doing something

for themselves. I think Dr. Keidel has brought up a serious question, and the sooner we realize it and look it squarely in the face the better it will be for all concerned.

Dr. J. Frank Schamberg, Philadelphia: I am entirely in sympathy with the trend of the remarks made by Dr. Keidel and Dr. Cole. I believe it is most timely that a paper on the economics of the treatment for syphilis and venereal diseases should be brought before medical bodies, for the medical profession must at this time either provide cheaper and better medical treatment or else this will be taken out of our hands and we will be directly facing state medicine. Most physicians are emotionally opposed to state medicine, and it may be that by some changes from within we may be able to prevent it. It was something in the nature of a surprise when the British medical profession, that so bitterly opposed the panel some years ago, made definite proposals to the British Government in 1930 to socialize the entire practice of medicine in England. I have long felt that the general profession commercialized too much the treatment for venereal disease. I have long told my students that they have no right to charge larger fees for venereal diseases than the patient can afford to pay. The duration of treatment will be in inverse ratio to the amount charged for medical services. If a millionaire is being treated for syphilis we need not be so circumspect, for a physician is doing a great service in preserving his life and health, and is entitled to a generous remuneration. Seventy per cent of the patients with syphilis are treated by the general practitioner, and we should endeavor to see that they are treated skilfully and within their means. We should see that their treatment is not commercialized, and we as a national body can bring our influence to bear on the medical profession in this very important matter.

Dr. Howard Fox, New York: Of the author's four recommendations to solve this difficult problem, the first three can, I think, be carried out without great difficulty. The pay clinic, however, represents a problem that has caused much hostility and resentment in the medical profession. I refer to clinics that cater to the so-called white collar class and that charge a considerable fee. Strictly speaking, most dispensaries except municipal ones charge some fee, though this is usually small.

I have been greatly interested in the question of pay clinics through my connection for several years with the Committee on Dispensaries of the New York County Medical Society.

The Society has gone on record more than once as being opposed to pay clinics in general, and particularly in regard to therapeutic activities. At a recent meeting of my Committee on Hospitals and Dispensaries, the question of syphilitic pay clinics was discussed, the unanimous opinion of those present being strongly opposed to them. The opinion is widely held in New York that many physicians would be willing to reduce their fees to meet those charged by pay clinics and that the work could be done as efficiently. Some think that the establishment of pay clinics for syphilis would be followed by similar experiments in all other branches of medicine and that this would have the disastrous result of eliminating the general practitioner. The majority in New York City are firmly convinced that this is another step that is rapidly bringing us to state medicine.

Dr. Samuel Sweitzer, Minneapolis: This problem of syphilis is not so simple as it seems. One phase of the problem is urban and the other is rural. We can do a great deal for syphilis in the large cities by pay clinics and whatnot, but this cannot be done in the rural districts, and if we depend only on one type of treatment we will not get anywhere. The general doctors in the towns and cities

will have to take care of a certain number of patients, and that will continue to be so unless there is a socialization of medicine. We have in Minneapolis practically a free clinic where any one who is without funds can be treated, and at the University they make a very small charge. We also hospitalize these patients so as to isolate them from the public and prevent spread of the disease in the acute stage. You will remember if you read the report of the clinic in Chicago that the statement was made that at one time they ceased advertising and their business fell off so markedly that they had to start advertising again. That clinic, I am sure, would not be so successful if they did not continously run their large advertisements.

Dr. Jeffrey C. Michael, Houston, Texas: I am not satisfied that syphilis is any more of a public health problem than other contagious diseases. The syphilitic patient has been exploited more by the rank and file of the medical profession than the man with arthritis, for example, and in that respect we will have to clean house. I am not in favor of the profession approving the treatment of syphilis as a public health matter, without regard for the patient's economic status. That means the beginning of state medicine. If syphilis is going to be managed in that way, there is no reason why other diseases will not be, and if you want state medicine the way to get it is to encourage what has been proposed here.

From a selfish standpoint, state medicine may be a very good thing for the well established specialists. I can conceive of a system in which they would be in a position analogous to the proprietors of high class private schools. They would cater to the well-to-do only, receiving large fees for highly individualistic service. But the great mass of the medical profession and the public would be in no such enviable position, and it is of them that we must think.

Dr. George M. MacKee, New York: Of course, the poor will go where they wish, but the middle class, those persons who have considerable pride and hesitate to have it known that they have syphilis, do not like to go to syphilitic clinics, and often they cannot afford to go to the private office of a specialist. The combination of a dermatologic and a syphilitic clinic is a help, for many persons do not hesitate to go to a dermatologic clinic for treatment for their syphilis. If such a clinic has a proper social service system, the patient can be followed up just as well as in the regular syphilitic clinic. If there is not going to be state medicine, we might advocate these combined clinics rather than to create too many purely syphilitic clinics.

Certainly we should make the cost of the treatment for syphilis as low as possible. In many clinics the expense to the patient is considerable. In my clinic the patient has to pay fifty cents to get in and an additional charge for mercury, arsenic or anything he gets, so in all the cost is probably as much as he would pay a family physician. I think the reason most patients go to such clinics is because they feel they are being treated by specialists rather than by a family physician and have a better chance for cure. It is possible that much good can be accomplished by educating the family physician in the general management of syphilis, using the syphilogist as a consultant.

Dr. Frank W. Cregor, Indianapolis: I feel that the medical profession is in custody of its own destiny, and likewise responsible for its own ills. I have felt that the medical profession should present to the public its attitude on this disease that so vitally affects the public health. Really, there is no body of men so qualified to speak to the public on this question as this body. Are there any other professions that may reflect the attitude of the syphilologist on this great question?

I have often thought that if the medical profession knew half that the public thinks it knows, it would really be a very wonderful profession. I believe the public is eager for this information. I have sat in meetings where the question of the reporting of venereal disease has come up and has been almost ruthlessly turned down. That is not constructive criticism, and who is so well qualified as the medical profession to give constructive criticism? We are disposed to reflect individual views, and the medical profession in reflecting individual views makes many mistakes. The medical profession in reflecting its consensus will not make a mistake. I believe that there should be some way in which the views of this collective body should be communicated to the public, and we should lead in helping these lay organizations, which will be amenable to our influence, if we will just show them the way.

The thought I wish to leave is this, that such a body as this should give to the public information that would represent the consensus of the medical profession, and that it should exercise great care to the end that any criticism of lay or philanthropic organizations' activities along the lines of cure and control of venereal diseases be constructive in character. I would be pleased to see it take steps to provide officially for a committee with such duties in mind.

Dr. Keidel's paper is timely, and I wish to express appreciation to him for presenting it. We are all acquainted with these problems as they present themselves in our local communities. Individual physicians, as well as lay organizations, need help if they would at all times act in keeping with medical ideals and not run counter to, and find themselves in conflict with, the priniciples of medical ethics, which applies to universities, clinics and institutions, as well as to the individual physician. In my opinion, the organization should supply that helpful information, and I sincerely hope that it takes steps to do so.

Dr. Joseph Grindon, St. Louis: I am quite in accord with Dr. Michael when he said the problem of syphilis is the same as the problem concerning other diseases. At bottom it is the same. It is a calamity for a man in moderate circumstances to contract syphilis. It means great expense, but the same is true of other conditions. Does pneumonia or does a broken thigh ever come at a convenient time? No. How many have a fund put aside to take care of any illness? Very few, yet the matter is eventually settled, for there is a modus vivendi arrived at between the doctor and the patient, and that is a matter which must be left to the individual doctor. Some years ago in St. Louis a committee was appointed to examine and to report on the conduct of clinics and hospitals in their financial relation to the public. They did a great deal of work and were in session for a long time. Finally they reported in substance that they had come up against a stone wall, and that the matter should be left where it had always been, in the hands of the practitioner, whether singly or organized into groups. The great majority of the medical profession are philanthropists. They want to treat their patients justly and mercifully. No other body of men is so philanthropic. Nevertheless, in some instances, through cupidity, charges for the treatment for syphilis are excessive. As to the man in middle circumstances—what about him? Each of us has his own way of dealing with the problem. Mine is something like this: A man comes in and asks, "What will you charge me for a shot of 606?" I tell him, "Nothing. I will give it and furnish the medicine free. I will charge you so much for six months' treatment, and whether I give you shots or pills is my business. After that we will arrange again." He may say, "I cannot afford to pay that price." I then consider with him what he can pay without unduly impoverishing himself. Perhaps he can do without a car, without a radio, or

something, and by making certain sacrifices can pay me a fair fee. I think it should be left to each of us to judge what our charge shall be, and what expense is proper for a $2,500 man, a $1,500 man, and so on.

DR. HARRY G. IRVINE, Minneapolis: I should like to say just a word on certain aspects of this question. I had quite a lot of experience during and after the World War on the public health side of the control of syphilis, and I think this problem as it presents itself is a great test of how far we, as a profession, are willing to go to support our ideals concerning the stamping out of diseases. There is bound to be argument about the cost of pay clinics and so on, but I have reached the conclusion that if syphilis and gonorrhea are ever to be stamped out it will have to be done through some definitely organized movement. It is all very well to talk about the pay clinic, and to talk about the private physician and so on, but we are dealing with a condition different from ordinary diseases. If a patient has pneumonia he is sick; if he has a broken hip he is sick and he must be cared for, but the man with syphilis is not ill from the standpoint of incapacitation. He can stop treatment at almost any time, and no one knows when he is going to become a menace to the public health. Leaving this in the hands of the physician will never get anywhere. I think that the medical profession will have to go on record as to whether they are willing to back up the things they have stood for in stamping out diseases. Dr. Sweitzer stated that the clinic in Chicago lost its business when it stopped advertising; this helps to prove my point that it must be a definitely organized movement that advertises and brings people for treatment. Most of these people must be told where to go, and how often, and must be directed in some way so that they will be attracted to the clinic if anything is to be gained.

DR. SAMUEL AYRES, JR., Los Angeles: The Los Angeles County Medical Society has recently gone into the question of pay clinics, free clinics and so forth, and one thing that appeals to me is that nothing revolutionary is proposed. The men are encouraged to develop their own clinics in their own offices by setting aside one or two evenings a week, or one or two mornings a week. Each man has his own equipment and his own assistants, and it is felt that it is preferable to utilize the equipment that is already at hand and bring in some revenue rather than to establish free clinics and let this equipment lie idle, which seems a reasonable point of view. Suppose a patient paid only $2 a visit, if there were enough of them it would justify setting aside certain hours for that particular class of patients. If the physician himself did not care to be in attendance, he has young assistants who could easily manage with proper supervision the handling of that problem. I feel like Dr. Michael and some of the others, that the idea of encouraging these persons to seek institutions is undesirable. I think that we should not place greater handicaps in the way of the young doctors.

DR. CHARLES D. FREEMAN, St. Paul: This subject I am a little hesitant to talk about as the medical professon has always reacted reluctantly to this phase of preventive medicine, namely, venereal prophylaxis.

If we had methods of prevention in such devastating diseases as carcinoma, tuberculosis and infantile paralysis, we would not hesitate to headline them.

Not so with venereal diseases. Here we have methods that if properly used are practically 100 per cent effective, and still we remain inactive. I do not know just what line of procedure we should take. If only the transgressor were the sufferer, there might be some possible reasons for our silence, but when we consider the number of innocent infections, it seems to me that we as a profession should take some definite stand in advocating methods we know to be effective.

DR. GEORGE M. MACKEE, New York: I wonder if something cannot be done in this country to offset the horror of this disease by education of the public. A great deal of harm is done, and many patients hesitate to let any one know they have the disease because the word syphilis is obnoxious to most people in this country. If the disease could be discussed among lay persons as is cancer and tuberculosis, the time might come when a person who contracts syphilis would not feel like a social outcast. I understand that this is the case in other countries.

DR. KARL G. ZWICK, Cincinnati: In some countries of Europe much of the stigma attached to syphilis has been removed by placing, officially as it were, the treatment for this condition on the same basis as the care of any other disease. The action of state and other insurance agencies of assuming the financial responsibility of the treatment for syphilis seems to have also solved, to a large extent, the economic problem connected with the disease. Furthermore, this action tends to obliterate as just indicated the line of distinction drawn between moral and immoral natural instincts.

DR. J. FRANK SCHAMBERG, Philadelphia: Apropos of the last speaker's remarks, I wish to state that a year ago I communicated with the head of one of the largest insurance companies and asked him whether he could not demand in agreement with other companies a Wassermann test before policies were granted. I said this not only would serve as a great educational factor, but that it would discover tens of thousands of persons who have ignored syphilis, and that they would learn this at a time when they could be helped. After consultation with others, he stated that this was not feasible.

DR. ALBERT KEIDEL, Baltimore: I am pleased to have had so much good discussion, but I cannot attempt to reply to everything that has been said. Some statistics have appeared that show that the annual rate of syphilitic infection is about 3.40 per thousand of the population each year. If we add this figure to those already infected, it is obvious that the incidence of syphilis in the population is well over 10 per cent. In a forthcoming paper, Parran makes the point that each year every 100 syphilitic persons give rise to another 100. In other words, syphilis is probably neither decreasing nor increasing but staying just the same year after year. We cannot rest satisfied with this situation. It is by no means a new one; it has been in the minds of most of us for many years, particularly since the World War. Ten or fourteen years have gone by, and we still have no solution of the problem. Syphilis is not in the same category as other infectious diseases. They are all contagious or infectious, but there is this difference, which I once pointed out at a meeting of the board of health in Baltimore. I said to the director, "You would not mind wearing a button in the lapel of your coat stating that you had tuberculosis, if the law required it. Would you object to wearing a button stating that you had gonorrhea or syphilis?" He said, "That is entirely different." That is the problem. The same public health measures cannot be used as for pneumonia, tuberculosis or typhoid fever.

PERSISTENT NODULES IN SCABIES

HISTOLOGIC OBSERVATIONS AND TREATMENT *

SAMUEL AYRES, JR., M.D.
AND
NELSON P. ANDERSON, M.D.
LOS ANGELES

Our purpose in this paper is to call attention to a complication of scabies consisting of the occurrence and persistence, after thorough treatment, of pruritic pea-sized nodular lesions. These persistent nodules occurred in five cases of scabies which we have observed during the past year and a half. The lesions have varied from the size of a small to that of a large pea, have been red or brownish red, and have always been definitely infiltrated, and where the skin was loose as on the penis, they could easily be picked up between two fingers. In all cases they were intensely pruritic. Many of the penile lesions showed a definite central depression, and in several cases they seemed to subside only to recur in the same and other locations.

With the following exceptions, a careful search of the voluminous literature pertaining to scabies failed to reveal any mention of this type of lesion. According to Ormsby,[1] "In many cases comparatively large inflammatory papules occur which may remain for a long period even with treatment, These are usually seen on the scrotum, penis and about the elbows but occur elsewhere. In these the acarus may be demonstrated comparatively deeply in the lesion." Speaking of lesions on the penis, Montgomery [2] stated "At times the scabetic papules are well raised, rounded, circumscribed, firm and resemble the papules of early constitutional syphilis." It is not at all clear that Montgomery referred to the persistent type of lesion described in the present report. Clark and Stibbens [3] called attention to the fact that "partially treated scabies may show remains of lesions about the genitals that are flattened papules and in association with these are enlarged lymph nodes that

* Submitted for publication, May 25, 1931.

* Read before the Dermatology and Syphilology Section of the California Medical Association at the Sixtieth Annual Session at San Francisco, April 28, 1931.

1. Ormsby, O. S.: Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 1039.

2. Montgomery, D. W.: California State J. Med. **7**:53 (Feb.) 1909.

3. Clark, T. J., and Stibbens, F. H.: California & West. Med. **32**:26 (Jan.) 1930.

would lead the unwary to mistake the picture for genital herpes or possibly a primary case of syphilis."

REPORT OF CASES

CASE 1.—Mrs. C. M. had had an itching eruption for about four months and gave a history of contact with a friend who was similarly affected. Two months before she was seen by us a sulphur ointment had been prescribed, but she had applied this only to the buttocks for a period of one month. She stated that she had had the nodules before using the sulphur ointment, and that after using the ointment the nodules had disappeared but had recurred. About five days before she

Fig. 1 (case 1).—Persistent nodules of scabies on the posterior part of the thighs.

was first seen another physician had prescribed what was evidently an effective antiscabetic ointment.

On examination there was an ill defined dry chafed appearance of the anterior portion of the abdomen and sides of the trunk apparently due to the medication. Scattered over the buttocks (fig. 1) and anterior axillary regions were from six to ten pea-sized, red brown, itchy nodules. A nodule was completely excised for study, and the patient was given 4 one-quarter skin units of unfiltered roentgen rays to the affected regions, together with a soothing lotion. At the end of this time the lesions were practically flat, but one week later they were all much worse again and stood out as distinct inflammatory nodules. No other evidence of scabies was present at this time. We then injected the lesions with procaine hydrochloride and fulgurated them deeply with unipolar current. Shortly after one new lesion developed but two weeks later it seemed entirely well.

Case 2.—Mr. J. W. T., referred by Dr. La Grand Noyes of this city, had had an itchy generalized eruption of three months' duration. He had applied various combinations of sulphur including a proprietary antiscabetic ointment.

Examination revealed a blotchy erythematous dermatitis of the body, apparently due to the medication. The penis presented six or eight definite pea-sized nodules, especially about the foreskin (fig. 2). There were several similar lesions on the scrotum and one on the buttock. One of the penile lesions was completely excised for study. After one roentgen treatment to the penis of one-quarter skin unit, a new crop of typical scabetic lesions developed on the body, and the patient was given a suitable ointment. He did not return for further observation. On April 9, 1931, nearly four months from his last visit, he reported by phone that the nodules on the penis were still present and very itchy—this in spite of repeated applications

Fig. 2 (case 2).—Persistent nodules of scabies on the penis.

of scabies ointment even when bandaged on. He said that there were no lesions elsewhere on the body.

Case 3.—Mr. E. B. had had a generalized pruritic skin eruption of six weeks' duration for which various ointments, light treatments and intramuscular injections had been given. For two weeks previous to the time that we saw the patient he had been applying sulphur ointment and taking sulphur baths. He presented about a dozen erythematous nodular lesions having a slight central depression. These were located on the axillary folds, buttocks and penis. He was given a strong antiscabetic ointment consisting of:

	Gm. or Cc.
Betanaphthol	8
Sublimed sulphur	16
Balsam of peru	60
Petrolatum	60

This resulted in marked improvement, but the lesions on the buttocks and penis persisted. About two months after we first saw him his wife became affected, and they were both advised to repeat the foregoing treatment. The lesions improved again but did not entirely disappear, after which we gave 4 one-half skin units doses of roentgen rays unfiltered to these persistent nodules, about two weeks apart. Five months after we had first seen him he developed several pinhead-sized lesions on the body quite suggestive of active scabies, and for the third time the foregoing treatment was instituted. Ten days later two of the lesions, one on the left side of the umbilicus, the other in the inguinal region, were anesthetized with procaine hydrochloride and curetted deeply followed by light desiccation with the monopolar current. About ten months later, the patient reported by phone that the lesions that were destroyed by electrodesiccation healed in about three weeks and that he had had no further trouble.

Case 4.—A young white woman complained of a generalized itching eruption of eight weeks' duration, which developed after a friend who was similarly affected had visited at her house. The patient's sister was also affected. Adequate treatment for scabies had not been given although various applications including salicylated ointment and baths in compound solution of cresol had been used.

Examination revealed a few coin-sized erythematous wheal-like lesions on the anterior aspects of the thighs. There were no lesions on the face. A few papulovesicular lesions were noted on the fingers. Typical papulovesicular lesions were scattered over the trunk with especial predilection for the buttocks, hips and breasts. The patient was given an ointment containing 6 per cent sulphur precipitate in lard, with instructions for its proper use and for the sterilization of clothing. One month later the patient returned with the eruption still active. She was then given the same prescription used in case 3, the ointment to be applied to the entire body for three nights.

Ten days later, the eruption was entirely gone except for a few persistent pea-sized nodules on the buttocks. She was given a bland lotion. Five months later the patient was seen again; about a dozen nodules on the buttocks and leg were still present, although there was no other evidence of active scabies. The patient stated that the nodules would become quiescent at times, only to flare up again especially after friction such as walking or prolonged riding. They were intensely itchy. A nodule from the leg was excised for histologic study.

Case 5.—A Mexican boy, aged 1½ years, had a typical scabies of two weeks' duration. A 4 per cent sulphur precipitate in lard was prescribed to be applied for four nights. Two weeks later the scabies was entirely well, but scattered over the trunk and buttocks were from ten to twelve small pea-sized red lesions which the mother stated were quite itchy. The mother was advised to use the foregoing ointment on these lesions only for five days. Three weeks later the mother reported that the boy was entirely well. These lesions did not persist as long as in the other cases cited. From a clinical standpoint, they were identical with the persistent nodules in our other cases. While strictly speaking this case may not belong in the same group as the other four, yet it is included simply for the purpose of showing that borderline or transitional types of persistent nodules occur.

HISTOPATHOLOGY

Serial sections of an entire excised nodule were made in an effort to determine whether or not Acarus scabiei, its ova, larvae or feces were present in the lesions. In two cases in which this was done we

were unable to identify the parasite or any portion thereof. The essential histologic findings were as follows:

In case 4 in which the nodule was excised from the inner surface of the leg, the section consisted of a rather marked perivascular round cell infiltration throughout the cutis but most marked in the middle and deep cutis. The papillary and subpapillary zones presented only a moderate cellular reaction and some interstitial edema. The epidermis was practically unchanged except for evidence of slight irritation (fig. 3).

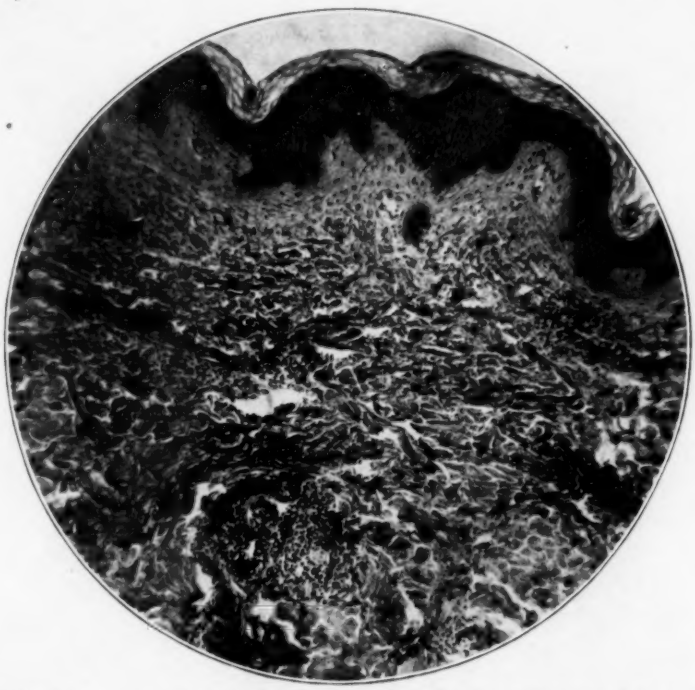


Fig. 3.—Low power view in case 4, showing marked cellular reaction, composed mostly of round cells. The reaction is mostly perivascular especially in the deep cutis.

In case 1 in which the entire nodule was excised but through error only five sections were made, the histologic changes were quite similar to those of case 4 as previously described, although somewhat more marked in degree.

In case 2 the histopathologic changes were quite striking. The epidermis presented evidence of marked irritation with pronounced intracellular edema and vacuolization of the prickle cells. The entire cutis presented a marked cellular infiltration. In the upper and middle cutis this cellular infiltration consisted practically entirely of plasma cells

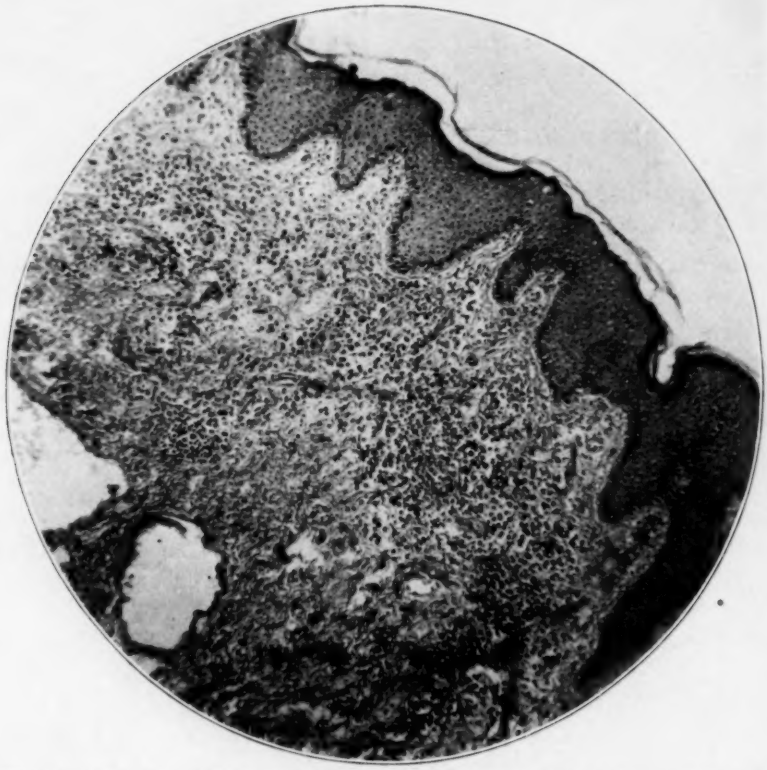


Fig. 4 (case 2).—Vacuolated epidermic cells and marked edema of the cutis with considerable cellular reaction. On high power magnification (fig. 5), these cells are seen to be plasma cells.

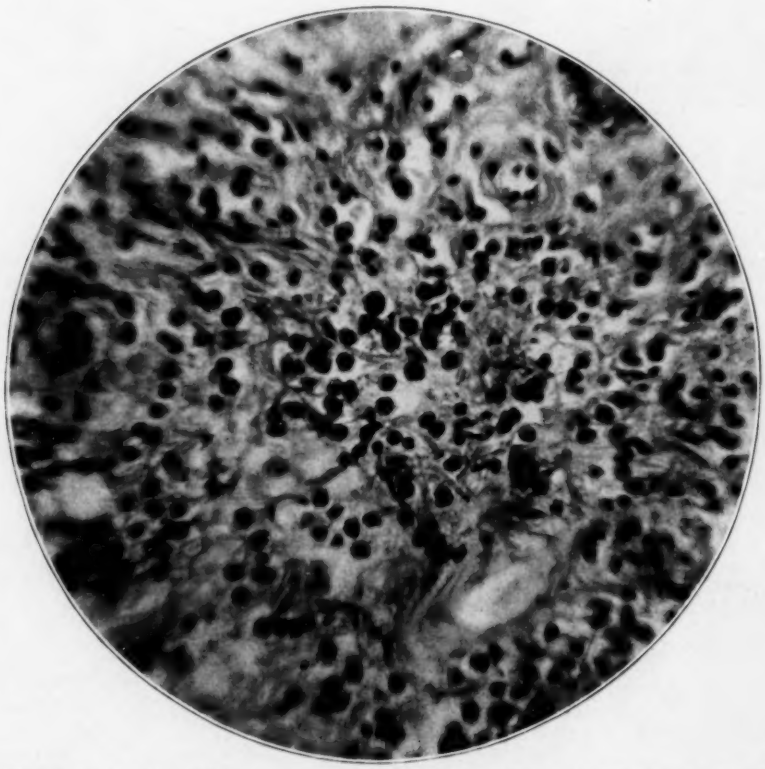


Fig. 5 (case 2).—High power view of cellular infiltrate in figure 4, showing the practically pure plasma cell infiltrate.

Fig. 6 (case 2).—High power view of the epidermis in figure 4, showing vacuolization of the epidermic cells.

Fig. 7 (case 2).—Perivascular round cell infiltrate in the deep cutis.

located in a markedly disorganized and edematous connective tissue and without any particular relationship to blood vessels which were markedly dilated as were also the lymphatics (figs. 4, 5 and 6). In the lower cutis the cellular infiltration was predominantly perivascular and consisted mostly of round cells with a few plasma cells (fig. 7).

Essentially then, the histopathologic changes in two cases consisted of a marked perivascular cellular lymphocytic infiltration in the mid cutis and deep cutis. In another case, in addition to the foregoing, a practically pure plasmoma [4] was present in the upper cutis. No parasites, larvae, eggs or feces were identified in any of the sections.

COMMENT

In ordinary scabies, according to Unna,[5] the itch mite burrows obliquely into the horny layer until it reaches its base and then makes its way inside the central horny layer, parallel to the surface, forming in this way burrows. The penetration of the mite itself into the prickle cell layer is improbable even on clinical grounds. In the prickle cell layer all the changes from early to late vesicle formation are seen. Regarding the changes in the cutis, Unna merely mentioned a more or less pronounced edema of the papillary body, the blood vessels of which are dilated and the fixed connective tissue cells are enlarged and multiplied, although in a figure illustrating the pathologic process of scabies he used the term "plasmomatic infiltration" in connection with the cellular reaction in the cutis.

From a histologic standpoint, we are unable to explain the occurrence of such nodules. Are they due to a variety of Acarus that is exceedingly resistant to treatment? Are they caused by a more virulent type of Acarus, which instead of stopping and sojourning in the horny layer, dig themselves deeper into the prickle cell layer and thus avoid contact with antiparasitic remedies? The predilection of such persistent nodules for the shaft of the penis, inner surface of the thighs, anterior axillary folds and buttocks would suggest that the thinness of the skin in these areas might have something to do with their formation and location. Could these nodules represent a persistent toxic reaction of the tissue to an organism that has already been been eradicated by treatment? Or could it be that the Acarus under certain

4. Bonaduce, F.: Rare Symptomology in Scabies Caused by Sarcoptes Hominis, Dermosifilografo **2**:399 (Aug.) 1927. This is a rare type in which the ears, nose, temples and eyebrows were involved in addition to other areas. Histologic studies were quite similar to ours, and Bonaduce concluded that Sarcoptes is capable of causing a granulomatous reaction (Sarcoptic Granuloma?). He, however, found the parasites actually present in his sections.

5. Unna, P. G.: Histopathology of Diseases of the Skin, Walker's translation, New York, The Macmillan Company, 1896, p. 162.

unknown conditions deposits her eggs deeper in the epidermis than usual, thus giving rise to a reaction akin to a granuloma and creating a focus from which at various times matured mites issue forth again to attack the host and cause a recrudescence of the disease?

The histopathologic changes do not at all suggest that the Acarus has burrowed into the epidermis more deeply that usual. If such were the case one would expect to find vesicles in the prickle cell layer. The lodging of an Acarus in a hair follicle with subsequent deposition of the ova might possibly occur but in such a case the lesions should be distinctly follicular. Such a condition actually occurs in "camel itch," a disorder due to a parasite similar to but smaller than Acarus scabiei. In "camel itch," according to Dyson,[6] the parasites were found within the hair follicles, but the lesions are follicular papules found chiefly on the arms, chest and legs. There is nothing, however, in the histologic picture of any of our cases to suggest follicular pathologic changes.

The diagnosis of such lesions does not offer any particular difficulty, especially if the history of an antecedent or concomitant scabies is obtained.

TREATMENT

Ordinary antiscabetic treatment seems incapable of coping with these persistent nodules. This does not imply that all scabetic cases with papular or nodular lesions will resist treatment, since such lesions are very common about the genitals, buttocks, axillae and umbilicus. But we do feel that patients in whom nodular lesions in these locations persist in spite of adequate and possibly repeated applications cannot be made to respond by a continuation of such therapy. In fact, the persistent nodules in several of our cases have become distinctly more inflamed by repeated inunctions of sulphur preparations. We believe that complete eradication of such lesions can be accomplished only by heavy electrodesiccation or coagulation and curettement under local anesthesia.

SUMMARY

1. Persistent nodular pruritic lesions which resist the usual sulphur medication may occur as a complication or sequela of scabies.

2. Five cases are reported in which such a complication occurred.

3. Serial sections of excised nodules in two cases failed to reveal the presence of parasites, ova, larvae or feces. In two cases, there was a marked perivascular lymphocytic infiltration of the middle and deep cutis, and in another case there was, in addition, a marked plasma cell infiltration.

4. Electrodesiccation or coagulation followed by curettement seems to be the treatment of choice.

6. Dyson, W.: Brit. J. Dermat. **33**:107, 1921; quoted by Ormsby (footnote 1, p. 1046).

UNUSUAL CLINICAL MANIFESTATIONS FOLLOWING INTRAVENOUS ADMINISTRATIONS OF GOLD COMPOUNDS *

BINFORD THRONE, M.D.

JEROME KINGSBURY, M.D.

AND

C. N. MYERS, PH.D.

BROOKLYN

Since the introduction of gold compounds in the therapy of tuberculous conditions about fifteen years before this article was written and their subsequent application to other conditions, especially dermatologic, many reactions have been reported. These have varied from simple pruritus and erythema to reactions that have proved fatal.

It was our purpose, after about five years' experience with these preparations, to review the reports of cases showing these untoward symptoms following their intravenous use. However, as Driver and Weller [1] recently published an extensive survey covering this subject, our report will only briefly summarize the types of these reactions; such points as seem to us to be of special interest will be discussed and our own experiences given.

According to Driver and Weller, the various types of reactions are:

1. Immediate reactions: (*a*) The anaphylactic type is characterized by various degrees of syncope and shock, associated with nausea, and at times with vomiting, flushing and edema of the face, etc. These symptoms may disappear after a few minutes or may result fatally as in Bruhns' [2] case. (*b*) A mild febrile reaction occurs with malaise and headache, lasting from a few hours to several weeks. (*c*) There is a metallic taste in the mouth. (*d*) Reactions to colloidal gold with a protein protector are noted. These seem to be due to the protein.

2. Delayed toxic reactions: This group contains the largest number of cases, and the reactions usually occur after the second or subsequent injection. The symptoms may begin as early as from four to six hours after the injection and last for periods varying from a few hours to many weeks. Albuminuria is practically always present.

---

* Submitted for publication, May 20, 1931.

* From the New York Skin and Cancer Hospital.

1. Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, Arch. Dermat. & Syph. **23**:87 (Jan.) 1931.

2. Bruhns, C.: Dermat. Wchnschr. **95**:945, 1924.

Stomatitis and gingivitis of varying degrees have been seen frequently. Hepatitis with an associated icterus has been noted. Digestive disturbances are extremely common.

3. Reactions involving the skin: These vary greatly in character, severity and type, and resemble closely those caused by other heavy metals, especially arsenic and mercury. They are always associated with pruritus. The most serious of these are the pemphigoid and universal exfoliative dermatitis types, either of which may lead to a fatal termination unless proper eliminative treatment is instituted at once.

A unique and rare type of cutaneous reaction not mentioned by Driver and Weller was seen in a case shown by Best [3] at a meeting of the Brooklyn Dermatological Society and observed by one of us (B. T.). Best showed two cases of lupus erythematosus. Both patients were white women; one had received intravenous injections of gold and sodium thiosulphate, and the other had received neoarsphenamine. Each woman showed patches clinically identical to those of lichen spinulosus; the location, extent and intensity of the cutaneous involvement was practically the same in each patient.

Focal reactions in the lesions of lupus erythematosus are frequently seen. They resemble the Jarisch-Herxheimer reaction. In tuberculosis of the skin the development of lesions simulating tuberculids has been reported. Bloch [4] stated that he had seen severe reactions in Swiss sanatoriums for tuberculosis, and that the applications of gold preparations provoke the formation of tuberculids, which he considered a strong proof that latent foci of tuberculosis are aroused. Pusey [5] stated that he had seen the same reactions. Gonzales Medina [6] reported a case of lupus vulgaris in which cold abcesses (suppurating adenopathy) and papulonecrotic tuberculids of the hands developed during active treatment with triphal. He considered the reaction partly the Jarisch-Herxheimer reaction seen with remedies that have practically a specific action, like tuberculin and arsphenamine. Weiss [7] reported enlargement of the lymph nodes in a woman aged 27, while under treatment.

Activation and dissemination of the lupus erythematosus process particularly in cases of the disseminate, and occasionally in those of the discoid, type have been reported. Hemorrhages into the skin

3. Best, W. H.: Lichen Spinulosus with Pigmentation Following Arsenic, Arch. Dermat. & Syph. **21**:1056 (June) 1930.

4. Bloch, Bruno, in discussion of Zeisler: Lupus Erythematosus, Arch. Dermat. & Syph. **18**:974 (Dec.) 1928.

5. Pusey, in discussion of Zeisler (footnote 4).

6. Gonzales Medina, R.: Acta dermo-sifil., April-May, 1928, p. 363.

7. Weiss, R.: Lupus Erythematosus Disseminatus Treated with Gold and Sodium Thiosulphate, Arch. Dermat. & Syph. **18**:447 (Sept.) 1928.

and from the mucous membrane, lungs, stomach and uterus have been reported. Miscarriages have been frequent.

4. Deaths: In addition to the death reported by Bruhns, Driver and Weller gave references to forty others, sixteen of which occurred in patients suffering from lupus erythematosus and the others in cases of tuberculous infection. They also referred to the work of Würtzen, who stated that treatment with sanocrysin resulted in death in 18 per cent of cases. An analysis of these deaths shows that a large number were in all probability caused by excessively large doses of the drug. A general examination of these patients for focal infections does not seem to have been made, nor a chemical analysis of the blood.

In all of the cases mentioned there were no symptoms that could be caused by gold or its salts alone. All of the different types of cutaneous reactions, from simple erythema to the bullous and the purpuric types and the hemorrhages from the mucous membranes of the mouth, lungs, gastro-intestinal tract, kidneys and uterus can be caused by other heavy metals, such as mercury, arsenic, lead and bismuth; the pathologic changes found in the kidneys, liver and spleen have been noted after poisoning by these metals. In other words, such symptoms are not specific for gold poisoning, but represent a group reaction. However, one sequela, a permanent type of staining of the skin, is peculiar to gold. Weller and Driver referred to two cases of this type; one reported by Schamberg and Wright and one by Zimmerli and Lutz. In addition, Beaumont [8] reported that a patient treated with sanocrysin after a sojourn in Switzerland showed staining on the exposed parts, which appeared blue as if from cold. Beaumont stated that he had heard of two similar cases.

Felix Savey [9] reported a similar case. In his patient the discoloration was particularly noticeable on the posterior aspect of the neck, just above the collar, and also on the lips. A troublesome dermatitis had developed all over the body, except on the hands and face, after a series of small doses of sanocrysin totaling 1.85 Gm. The last dose of 0.35 Gm. was given on September 28, and the discoloration was first noticed about three weeks later. A case of intense generalized pigmentation was reported by Jäger and Kohl [10] following injections of triphal. In this case the presence of gold in the skin was demonstrated by Dr. H. Brunotte. This case will be discussed later.

Our experience with gold compounds began during the summer of 1926. Tests for toxicity were carried out by Dr. C. W. Hooper on

8. Beaumont: Brit. M. J. **2**:818 (Nov. 3) 1928.

9. Savey, Felix: Brit. M. J. **2**:962 (Nov. 24) 1928.

10. Jäger, B., and Kohl: Grundsätzliche Erwägungen im Anschluss an einen Fall von Golddermatitis (Triphal), Arch. f. Dermat. u. Syph. **154**:76, 1927.

triphal, krysolgan and gold and sodium thiosulphate. Triphal was selected on account of its being the least toxic of the three compounds. In this connection it is interesting to note that among the deaths mentioned none seems to have been caused by this preparation, nor have we found any reference to a fatal result from its use in this country. It has been employed by us only in dermatologic conditions and chiefly in lupus erythematosus. In October, 1927, our results in the treatment for lupus erythematosus were reported,[11] together with the tests for toxicity. These tests showed that the maximum tolerated dose of triphal in the albino rat was 120 mg. per kilogram of body weight; that of gold and sodium thiosulphate was 60 mg. per kilogram of body weight, and that of krysolgan 2 mg. per kilogram. In the summary of the report it was stated that "advanced kidney and liver lesions seem to be the only absolute contra-indications to this type of therapy." Galewsky[12] stated that it should be used with care in cases that had a relation to sensitization to light. The reported cases of permanent staining of the skin justify his conclusion. It was also stated by us that focal infections should be cleared up before treatment was instituted.

Since the aforementioned report was made therapy with gold compounds has been used by us in 176 cases of lupus erythematosus, six cases of lupus vulgaris, one case of lupus pernio, the Besnier type, one case of angio lupoid, seven cases of erythema induratum, five cases of papulonecrotic tuberculid, one case of tuberculosis verrucosa cutis and one case of mycosis fungoides; about 3,500 injections have been given; all of the injections were of triphal except for a trivial number which were of aurophos (this preparation was discarded on account of its apparent chemical instability). Our doses have never exceeded 100 mg. three times a week, and for some time the maximum dose has been restricted to 75 mg., the average dose being 50 mg.

In addition to the cases mentioned seven patients with psoriasis have been treated and the results reported.[13] In the report of psoriasis it was stated that "The use of gold compounds in this disease should always be preceded by a blood chemistry. A high blood sugar and a low blood chloride are positive contra-indications for gold therapy," since it was found as the result of many thousand analyses of the blood that this change was absolutely indicative of retention of a heavy metal; the retained metal could be arsenic, lead, mercury or bismuth.

---

11. Throne, Binford; and Myers, C. N.: Treatment of Lupus Erythematosus with Gold Compounds, New York State J. Med. **27**:1064 (Oct. 1) 1927.

12. Galewsky, quoted by Throne and Myers (footnote 11).

13. Throne, Binford; and Myers, C. N.: Psoriasis: A Preliminary Report on Blood Chemistry Studies and Indications for Treatment as Shown by These Findings, New York State J. Med. **28**:914 (Aug. 1) 1928.

CONTRAINDICATIONS

To these contraindications the following are added, together with reports of cases that seem to justify our conclusions.

The acute disseminate type of lupus erythematosus is almost constantly associated with extensive focal infection, and shows all the symptoms of severe general sepsis.

In the list of deaths quoted by Driver and Weller was one fatal case reported by Gougerot-Burnier. Their patient was a man aged 29, who received 100 mg. of crisalbin; after eight days a second dose of 250 mg. was given, which was followed by a moderate reaction. A third dose of 250 mg. eight days later was followed by coma and death.

Hudelo and his co-workers reported a fatal case in a man aged 26; in one week he received 50, 70 and 50 mg. of crisalbin, each injection being followed by a mild febrile reaction. There was further dissemination of the disease. Then aurophos was given at two day intervals in the following doses: 0.001, 0.002, 0.005 and 0.01 Gm.; prostration occurred, and on the following day 0.003 Gm. was given. A generalized hemorrhagic eruption appeared, associated with coma. Death occurred two days after the last injection. Mitchell reported a fatal case after one injection. Stillians [14] reported a case in which a severe reaction with swelling of the liver developed after small doses. Gold therapy was discontinued, but the patient died.

In view of the marked sepsis that these cases show and the deaths quoted, it is our opinion that the use of gold compounds in this type of lupus erythematosus is absolutely contraindicated. If the general condition should improve and if demonstrable foci of infection can be removed, the temperature becoming normal and no further extension of the cutaneous symptoms occurring, gold compounds in very small doses, not exceeding 5 mg. of triphal, may be tried. During the acute stage, sodium thiosulphate can do no harm and may prove to be of benefit.

No patient with a true case of lupus erythematosus disseminatus acutus has been under our care since we began the use of gold compounds, but the following case could possibly be considered as belonging to this group.

CASE 1.—C. M., a white man, aged 36, an American, stated on his admission to the clinic that cutaneous lesions which had been present for eight weeks had developed after an attack of "rheumatism" involving the hips, knees and ankles. He also had had attacks of tonsillitis. Otherwise his history was of no significance. Examination showed a diffuse dark red pigmented rash with some infiltration, hyperkeratosis and scaling involving the greater part of the face (the cheeks, chin, nose and forehead). In some places the color was almost black.

14. Stillians, in discussion of Zeisler (footnote 4).

Behind the ears there were typical patches of lupus erythematosus covered with tightly adherent scales. On the dorsal surfaces of the hands and fingers there were lesions resembling those of erythema multiforme exudativum intermingled with which were patches covered with tightly adherent scales. The color of these lesions did not fade on pressure. The patient had marked dental sepsis; otherwise the general examination gave negative results. By mistake he was given 100 mg. of triphal, after which he had a severe reaction characterized by a chill, syncope and prostration which was so marked as to necessitate his being kept in the hospital. While in the hospital he had a typical septic course with elevation of temperature, etc. He was given sodium thiosulphate; his focal sepsis cleared up, and when he was discharged a few weeks later the lesions had entirely disappeared. Several months later, lobar pneumonia developed, and he died of cardiac failure.

In a previous article on the treatment with gold compounds,[11] of patients who have lupus erythematosus reactions associated with focal infections were reported as follows:

Case 2.—L. W., a woman, Jewish, aged 30, applied for treatment in July, 1918. Lupus erythematosus involved the nose, ears and skin just below the ears. The duration of the condition was approximately four years. Treatment previous to the use of a gold compound produced no clinical improvement. The patient received three injections of 0.1 Gm. of triphal on December 1, 3 and 6. She developed a papulovesicular rash on the arms, which became universal two days later. She received 0.5 Gm. of sodium thiosulphate in a freshly prepared solution, intravenously, on December 8 and 13. The dermatitis markedly improved. The patient received injections of 0.1 Gm. of triphal on December 13, 15 and 17. On December 31, the lupus erythematosus was pronounced cured. The patient had a marked dental infection which was cleared up at the time of the reaction. The total amount of triphal injected was 0.6 Gm.

Case 3.—Mrs. L. F., aged 32, had the typical butterfly type of lesions on the face, which had been present for eight years. The scalp was also involved. Treatment with a gold compound was initiated on October 6, and the dose was increased 0.05 Gm. on October 18. Eleven days later the amount was increased to 0.1 Gm. Following the last injection the patient developed an erythematopapular rash on the flexor surfaces of the arms and forearms. The rash spread to the trunk, thighs and legs. The pruritic condition was intense. Sodium thiosulphate, 0.5 Gm., in a freshly prepared solution was administered intravenously. On February 7, the reaction had completely subsided, and there was a slight recurrence of the lupus in the form of moderate scaly erythema. The dental infection was cleared up, and the patient was treated with a gold compound without further difficulty.

Case 4.—In John B., aged 41, lupus erythematosus lesions had been present on the nose and right cheek for five years. He had received a radium treatment without benefit and showed a marked dental infection, which was cleared up only on the development of a moderate pruritus following the triphal injections. Sodium thiosulphate therapy was instituted immediately, with prompt relief. The reaction developed after five injections of 0.1 Gm. of triphal given every third day. After the completion of the dental work, treatment with triphal was instituted with no untoward effect, and clinical improvement followed.

The following case is especially interesting in regard to focal infection and tolerance:

Case 5.—Mary M., aged 13, of Italian descent, had had an extensive involvement of the forehead, cheeks and ears for six months. She had received about fifteen injections of some gold compound, type not known, in another clinic before coming to us. This had proved ineffective. In view of the lack of response she was carefully examined and given injections of sodium thiosulphate for about two weeks. Triphal was then given in doses of 0.025 Gm. She showed extreme susceptibility and had frequent attacks of pruritus, which necessitated the discontinuance of this treatment. After nearly a year of these experiences, she appeared cured. After only a few weeks, there was a complete recurrence of the lupus erythematosus. The teeth were again examined roentgenologically, and an examination of the nose and throat was made, supplemented by roentgenograms of the sinuses of the head. A mucocele was found in one antrum and was removed. Culture showed a hemolytic streptococcus. Immediately following the operation there was a marked reaction in the lupus patches and the surrounding parts; they became acutely inflamed and swollen. On the subsidence of this reaction there was marked improvement in the lesions and a tolerance of gold therapy.

The foregoing cases show a definite intolerance in the presence of focal infection and the development of tolerance after its removal.

The following reaction was caused entirely by the use of too large doses.

Case 6.—In Mrs. M. F., Hungarian, aged 35, lupus erythematosus lesions of nine months' duration involved practically the whole of the nose and upper eyelid. Treatment with a gold compound was instituted on Oct. 6, 1926. Small doses were employed at first, with a gradual increase to 0.075 Gm. on October 25. On October 29 and November 5, 10, 12, 17 and 19, the doses were increased to 0.100 Gm. On November 24, the patient showed an erythematovesicular rash on the forearms and nose. Sodium thiosulphate in a freshly prepared solution was given intravenously three times a week until December 15, when all signs of reaction had disappeared. She received additional triphal in doses of 0.050 and 0.075 Gm., with prompt clinical improvement. On January 12 she was pronounced cured.

A reaction in lupus erythematosus in relation to carbohydrate metabolism is shown in case 7.

Case 7.—Mrs. T. B., a housewife, a Jewess, aged 49, was admitted to the clinic on Oct. 20, 1930. Lupus erythematosus had been present for about two months. Examination showed the typical butterfly type of lesion on the nose and cheeks together with extensive involvement of the forehead and ears and around the angles of the jaws. Examination for focal infection disclosed diseased tonsils and dental sepsis. Chemical analysis of the blood showed: chlorides, 511.6 mg.; sugar, 127.4 mg.; urea nitrogen, 16.7 mg.; uric acid, 3.84 mg., and carbon dioxide, 58.2 per cent by volume. The foci of infection were removed (by tonsillectomy and extraction of the infected teeth) after which triphal was given. On account of the hyperglycemia the doses were 0.025 Gm., except two that were 0.050 Gm. each. She received eleven injections in all. These were given three times a week. After the eleventh injection she complained of pruritus, and a maculopapular rash appeared on the face, neck, upper part of the trunk and shoulders. At that time analysis of the blood showed: chlorides, 462 mg.; sugar, 178.8 mg.; urea nitrogen, 14.4 mg., and uric acid, 3.12 mg. A comparison of this with the initial examination showed a drop of 49.6 mg. in the chlorides, an increase of 51.4 mg. of sugar and a drop of 2.3 mg. in urea nitrogen.

A similar case follows:

CASE 8.—Mrs. L. K., a white woman, aged 48, had suffered from an extensive lupus erythematosus of the scalp for nineteen years. There were also several small areas of the condition on the cheeks and ears. She had had diseased tonsils which had been removed before treatment was instituted. Chemical analysis of the blood on admission showed: chlorides, 453 mg.; sugar, 96 mg.; urea nitrogen, 15 mg., and uric acid, 2 mg. She was given two injections of 0.025 Gm. of triphal at three day intervals, and a third injection of 0.050 Gm. on the third day following. Three days after the last injection (Jan. 16, 1929) she complained of severe pruritus. On January 18, a widespread eruption of the type of erythema multiforme exudativum appeared. On January 16, analysis of the blood showed: chlorides, 437.7 mg.; sugar, 121.7 mg.; urea nitrogen, 8.9 mg., and uric acid, 2.8 mg., or a drop of 15.3 mg. in the chlorides, an increase of 25.8 mg. in the sugar and a decrease of 6.1 mg. in the urea nitrogen. On February 1, examination of the blood showed: chlorides, 429.3 mg.; sugar, 104.6 mg., and urea nitrogen, 12 mg. On February 15, the toxic rash had disappeared under the influence of injections of sodium thiosulphate, and on February 27, the observations on the blood were normal: chlorides, 462.7 mg.; sugar, 100.4 mg.; urea nitrogen, 16.4 mg., and uric acid, 2.8 mg.

This case is of special interest, because since reactions from heavy metals are accompanied by increase in blood sugar, it had been wrongly assumed that a decreased carbohydrate intake would probably prevent them, and the patient had therefore been put on a 10 per cent carbohydrate diet. After the reaction she was given a rich carbohydrate diet, which included as much candy as she wanted.

These two cases, together with those reported under psoriasis, according to our views, are perfect controls of the types of changes in the blood following reactions from heavy metals. In each instance a chemical analysis of the blood was made before treatment was instituted, and a comparison with the analysis made at the time of the reaction showed a marked reduction in the chlorides and an elevation of the sugar content. This was especially striking in the second case, in which there was an increase of 27.9 per cent in the blood sugar in spite of a very restricted intake of carbohydrates.

A decrease in urea nitrogen has been found especially in the acute stages of reactions to heavy metals. In our opinion, this is due to hepatic insufficiency, which is also shown by failure to store glycogen, the probable cause of the increase in the blood sugar.

In the first of these cases the high blood sugar content was in all probability due to hepatic damage, since a high amount of blood sugar caused by pancreatic deficiency (diabetes mellitus) may not be followed by reactions, as illustrated by the following case.

CASE 9.—Mrs. D. R., a woman, aged 41, a Jewess, had lupus erythematosus of the bridge of the nose and adjacent parts of the cheeks of about a year's duration. The family history showed diabetes. The blood sugar content was 143 mg.; the urine sugar, 1.48 per cent. The dextrose tolerance test showed a

definite diabetic curve. She was given triphal in doses up to 0.1 Gm. three times a week and did not show the slightest reaction.

It would seem therefore that in Pautrier's [15] case the use of insulin and a diabetic diet predisposed to the reaction.

The following cases recently seen by us showed unusual types of reaction. In case 10 there was a reaction in lupus erythematosus to a combination of ultraviolet light, heavy metal and gold and sodium thiosulphate.

CASE 10.—C. K., a white man, aged 40, was admitted to our service at the New York Skin and Cancer Hospital on Oct. 22, 1930. The past history was unimportant. The mother and father were living and well. Some members of the mother's family were tuberculous. Eight months previous to his admission to the hospital, there developed on the bridge of the nose an area of redness, which after two months spread to the forehead. He had received nine injections of gold and sodium thiosulphate in doses ranging from 25 to 100 mg.; also three or four injections of a bismuth compound. From the onset of the condition he had received treatment with "alpine light" (ultraviolet light) once a week up to the time of his admission to the hospital. The condition that he showed on admission had developed two weeks prior to that date. There was a disseminate patchy, squamous eruption on the trunk and limbs. On the face the lesions were moist and oozing. The palms were hyperkeratotic, and deep-seated vesicles were present. The lips and eyelids were involved. The urine was normal. There was no definite systemic disturbance. He responded readily to intravenous injections of freshly prepared solutions of sodium thiosulphate and was discharged practically well on Nov. 27, 1930. All treatment for the lupus erythematosus was given previous to his coming on our service.

Another case showing hyperkeratoses of the palms was as follows:

CASE 11.—G. W., a white man, aged 63, an American, had been given six intravenous injections of a colloidal gold compound for a supposedly malignant condition of the stomach. Two weeks after the last injection his palms became affected; on his admission to the clinic on Dec. 17, 1930, his palms were hyperkeratotic and showed the remains of deep-seated vesicles with markedly hyperkeratotic borders resembling closely the punctate keratoses seen after arsenic therapy.

Another ususual reaction was observed in a young woman with typical lesions on the face and ears. The patient received ten injections of triphal of 0.05 Gm. each. After this treatment she complained of loss of taste, i. e., inability to distinguish between salt and sugar. Treatment with sodium thiosulphate promptly cleared up this condition, with complete removal of the lupus lesions.

REACTIONS IN PSORIASIS

Our experience with gold salts in the treatment for psoriasis had led us to believe that it is of practically no value in this condition, and,

15. Pautrier, L. M.: Bull. Soc. franç. de dermat. et syph. **35**:282, 1928.

furthermore, that it is contraindicated. The use of heavy metals, arsenic, mercury and bismuth, for either external application or internal administration, is practically universal; a retention of any one of them predisposes to reactions that may prove serious. In the seven patients whom we treated [18] with triphal it was noticed that reactions of various degrees occurred. In two cases the reaction was extremely severe.

CASE 12.—X. Y., aged 23, had had lesions in large sheets on the trunk, limbs and scalp for three years. The palms, soles and nails had never been involved. Previous treatment had consisted of potassium arsenate, potassium iodide and sodium cacodylate. Externally, various ointments had been employed. In July, he was admitted to the New York Skin and Cancer Hospital and received six injections of 0.1 Gm. of triphal. On July 31, the patient complained of fever, headache, general malaise and a temperature of 103 F., lasting for nine days. During this period the patient developed stomatitis and gingivitis. The rash became very inflammatory and the skin was extremely edematous. Chemical analysis of the blood showed on August 7: sugar, 104.6 mg., and chlorides, 412.1 mg.; on September 19, sugar, 92 mg., and chlorides, 380 mg., revealing a marked alteration in the normal sugar chloride ratio. Injections of freshly prepared sodium thiosulphate were given, with prompt clearing of the psoriatic lesions as well as the other inflammatory processes.

In a similar case the patient had received injections of a bismuth compound previous to injections of a gold preparation. In this case the skin lesions also became universal, the palms and the soles becoming involved. In neither of these cases had there been any previous involvement of the palms and soles in respect to keratosis. In the other five patients who received the gold compound there was a reaction of some severity in each, as shown by the rash and by the pruritus. In each case there was an increase of the blood sugar, the highest amount being 130 mg., and in the blood chlorides, the lowest amount being 380 mg.

The aforementioned cases show clearly the tendency to reaction when there is a metallic retention, and they also exhibit in the chemical analysis of the blood that condition which has been called a metallic blood picture, that is, a change in the chloride-sugar ratio characterized by a lowering of the chlorides and an increase in the sugar.

A case similar to ours was reported by Jäger and Kohl.[10] Their patient was a woman, aged 33, who had suffered from psoriasis for ten years. The disease affected the areas of predilection. The authors obtained response to an intensive course of arsenic pills (Arsenpillen). For a recurrence a few months later a gold compound, triphal, was given at four to six day intervals, in a total dose of 0.46 Gm. After the fifth dose of 0.100 Gm. a transient pruritic exanthem appeared on the dorsal surfaces of the hands and fingers. After this disappeared, a sixth dose of 0.100 Gm. was given, following which a universal oozing dermatitis appeared, which finally assumed the form of an exfoliative dermatitis. The whole process was similar to arsphenamine dermatitis. The further

course of the condition corresponded to the case described by Ritter.[16] Hyperkeratoses were seen, and in addition scarlike atrophies with deeply pigmented borders and a lichenoid appearance. Severe hemorrhages, such as metrorrhagia, hemorrhages into the skin and mucous membranes of the mouth, bloody vomiting, etc., appeared. At times the blood picture was that of a lymphopenia with almost complete disappearance of blood platelets. The hyperkeratoses disappeared, but the pigmentation and atrophy remained. The histologic picture agreed closely with that of arsenic melanosis. Chemical examination of the skin by Dr. H. Brunotte showed the presence of gold. The interval between the last injection of triphal and the biopsy was nine months.

In Ritter's[16] case, a man aged 50, suffering from an inveterate psoriasis, received 0.5 Gm. of triphal in doses of from 0.05 to 0.1 Gm. during a period of twenty-eight days. On the day of the last injection the temperature rose to 38 C. (100.4 F.), and an erythema appeared which in a few days became universal, even involving the head and the face and resembling arsphenamine dermatitis with continued fever; new toxic exanthems with oozing and exfoliation of the skin appeared. After six months, the erythema had practically cleared up, but there had developed, chiefly on the back and on the arms, numerous follicular keratoses which by enlargement became confluent and disklike, ranging in size from that of a mark to that of a palm. They were brownish and resembled the hyperkeratoses seen at times after arsenic and also after arsphenamine dermatitis. Histologically, the condition was a chronic inflammation with hyperkeratosis. Examination for gold by histochemical staining gave negative results.

Saenz[17] reported a case of psoriasis in a man aged 42, who was given weekly injections of a gold compound (not named) in doses of 0.005, 0.008, 0.01 and 0.01 Gm. After the fourth injection there developed fever, headache, pruritus and an erythematovesicular dermatitis which later became eczematoid.

In the treatment of a patient with an obstinate case of psoriasis with triphal Schwartz[18] saw a mild urticaria appear after the third injection and increase in severity after the sixth injection. Later, a brownish discoloration developed in small and large spots over the whole body, with the exception of the face. This discoloration persisted for several months.

Kloeppel[19] reported severe collapse in a patient with psoriasis after the seventh injection of 0.075 Gm. of triphal.

---

16. Ritter: Dermat. Ztschr. **45**:158, 1925.
17. Saenz: Gold Dermatitis, Arch. Dermat. & Syph. **19**:319 (Feb.) 1929.
18. Schwartz, F.: Deutsche med. Wchnschr. **52**:535, 1926.
19. Kloeppel, F. W.: München. med. Wchnschr. **73**:1160, 1926.

Sáinz de Aja [20] treated a psoriatic patient with injections of triphal at three day intervals. Five injections were given in doses of from 0.01 to 0.05 Gm. They were followed by a severe reaction of an erythemato-urticarial type of a universal exfoliative dermatitis. The buccal mucous membrane was involved. The cutaneous condition lasted for forty days.

Pautrier [15] reported before the French Dermatological Society a case in a woman aged 49, who had been affected with this condition since her fourteenth year. Her blood sugar amounted to 150 mg. per hundred cubic centimeters of blood. The urine showed sugar. She was given a diabetic diet and injections of insulin. Thiocryasine was given in doses of 0.05 Gm. and then of 0.100 Gm. at five day intervals for three doses. The psoriasis was temporarily cleared up, but soon recurred, together with a discrete rash on the trunk which spread. The patient was admitted to the hospital. The temperature was elevated, and there was suppression of urine.

Hufschmitt [21] reported mild reactions in three of twelve patients with psoriasis treated with triphal and sanocrysin.

No claim is made that the cases mentioned represent the total number of psoriatic patients in whom reaction occurred on receiving gold compounds, but a fairly careful review of the literature failed to show others, and these seem to be sufficient to confirm our contention that gold preparations should not be used in psoriasis in spite of the favorable reports of Gordon.[22]

A résumé shows that eight authors, including ourselves, reported reactions, seven seeing extremely severe and dangerous symptoms develop from this type of therapy in psoriasis. All of the patients showed marked systemic symptoms, fever, chills, oliguria and an exfoliating dermatitis.

The following case of ours is reported to show that following injections of a gold compound a change in the chloride-sugar ratio can develop in a patient with psoriasis when a reaction occurs.

Case 13.—A. A., a woman, aged 48, a Jewess, had had psoriasis for several years. Chemical analysis of the blood before the use of a gold compound gave normal results. It should be stated here that the normal chloride content of the blood is considered to be 450 mg. per hundred cubic centimeters of blood, and the normal sugar content from 95 to 100 mg. The patient received fourteen injections of triphal in 0.05 Gm. doses. The injections were given twice a week. At first the condition improved, but at the end of these injections new lesions appeared, and she complained of pruritus. Analysis of the blood at that time showed: chlorides, 404 mg., and sugar, 130 mg. Injections of sodium thiosulphate were then given three times a week. At the end of three weeks the chlorides had

20. Sáinz de Aja, E. Alvarez: Rev. méd. Gallega, July 7, 1928, p. 193.

21. Hufschmitt, G.: Paris méd. **1**:91 (Jan. 27) 1927.

22. Gordon, Samuel D.: M. J. & Rec. **125**:548 (April 20) 1927.

increased to 437 mg., and the sugar had decreased to 93 mg. Two weeks later, the chloride content was 446 mg. and the sugar 100.4 mg. Treatment with gold compounds was resumed, and after two weeks the chlorides had again diminished to 437.7 mg., and the sugar had increased to 136.9 mg. There was no change in the diet during the periods when the gold compound or the sodium thiosulphate was given.

A case of psoriasis showing similar reaction and changes in the blood due to bismuth is as follows:

CASE 14.—In a man, J. B., aged 36, of Polish extraction, the blood was normal before treatment. After injections of bismuth for several weeks the chloride content was 432.7 mg., and the sugar 115.8 mg. Following injections of sodium thiosulphate, twelve days later, chlorides were 404 mg. and sugar 135.6 mg.; fourteen days later, chlorides were 421 mg. and sugar 84.6 mg.; seven days later, chlorides were 437.7 mg. and sugar 89.4 mg.

SUMMARY

All gold compounds are toxic, some more so than others. Their use is attended with danger, but this danger can be minimized by the following procedure:

1. The patient should be examined for focal infections, and one should remove such foci before instituting therapy with gold compounds.

2. A preliminary analysis of the blood should be made: (*a*) A high sugar and low chloride content means a physiologic dysfunction. This should be eliminated by a preliminary course of injections of a freshly prepared solution of sodium thiosulphate. (*b*) In cases showing a high blood sugar content not associated with pancreatic deficiency or metallic retention, the doses of the gold compound should be comparatively small. On the other hand, patients with definite diabetes mellitus seem to tolerate treatment with gold preparations.

3. The first sign of intolerance, as manifested by dryness of the mouth and pruritus, is an indication for discontinuance of the gold compound and the use of sodium thiosulphate. In our experience, these symptoms are invariably accompanied by an increase of the blood sugar, a decrease in the chlorides and frequently by a marked decrease in the urea nitrogen.

4. Chemical examination of the blood at weekly intervals, by showing an increase in the sugar and a decrease in the chloride and urea nitrogen content, frequently enable one to foresee an intolerance to gold compounds and, by instituting proper eliminative treatment at once, to prevent reactions.

5. It is impossible to determine previously the tolerated dose for each patient. The initial dose should be small, not exceeding 25 mg. of the gold preparation. This dose can gradually be increased if it is well

borne and is not effective, but it should be kept low as long as it shows a beneficial action on the lesions.

Positive contraindications for gold therapy are marked hepatic and renal disturbances, pregnancy, lupus erythematosus disseminatus acutus —the discoid type of lupus erythematosus which is becoming actively disseminated—and elevation of temperature. The same principle applies as well to cases in which previous damage to cells has been caused by focal infection as to those in which the damage has been caused by metals. It would seem that the seat of this damage is chiefly in the liver. The relative toxicity of the gold preparations described in our previous paper [11] seems to be substantiated clinically.

In psoriasis, treatment with gold compounds has been found to be of practically no value. A review of the cases reported shows a decided tendency to reaction, and in none of them could the doses be called excessively large. It is our opinion that it is due largely to previous metallic treatment which has caused damage to the cells. As Weiss [23] has expressed it: "In many living organisms one irritant leaves for a long time for following irritants, a greater capability of response; the irritability becomes increased. This shows for example that the second irritant, if it is of similar strength, has a greater action than the first or that a series of individually inactive irritants can exert an effect. This phenomenon is designated the summation of the irritants."

---

23. Weiss, Otto: Grundriss der Physiologie, part 2, Biophysik, Leipzig, Georg Thieme, 1925, p. 7.

HYGIOGENESIS OF WARTS DISAPPEARING WITHOUT TOPICAL MEDICATION*

KARL G. ZWICK, M.D.
CINCINNATI

"Not only must the truth be told, but also the cause of the error."—*Aristoteles.*[1]

The state of our knowledge concerning the response of warts to treatment is well described by Sir Norman Walker's remark, that: ". . . the ways of warts are mysterious, and they sometimes disappear in a few days under methods of treatment at which in the days of one's youth one was inclined to scoff."

Sir Norman refers to the observation, that: "Crops of warts will sometimes vanish under the apparent influence of minute doses of arsenic . . ., Epsom salts . . ., or green iodide of mercury . . ., and the disappearance of large crops has been noted to follow the injection of salvarsan."

But Sir Norman's remarks apply with, at least, equal force to the methods of treatment for warts by suggestion and irradiation, and more especially to the unorthodox mode of therapy by so-called magic, each of which is followed, at times, by the disappearance of flocks of warts.

In this paper I present an attempt to investigate the "mysterious ways" of the reaction of the warts to the methods of treatment just mentioned. As I had no intention to write a monographic review, I refer to the statements of the voluminous literature only so far as I think them pertinent to the problem discussed and so far as they have been accessible to me.

Being in charge of the practice of the venerable and esteemed Professor Augustus Ravogli, the observations were made in part on his patients, but largely on my own.

MAGIC THERAPY

Although modern man is inclined to make light of the doctrine of the curative transference of disease from one body to another or to inanimate objects through the supernatural power of magic, some of the therapeutic practices based on this doctrine are as popular in the folk medicine of today as they ever were in the Paleolithic Age. In my experience, this popularity is not confined to the mentally or otherwise underprivileged strata of society. On the contrary, I share the

* Submitted for publication, Feb. 8, 1931.
* Read at the Fifty-Fourth Annual Meeting of the American Dermatological Association in June, 1931, at Toronto, Canada.

1. Nikomach. Ethik. vll, 15 p. 115, 4a, 22.

opinion of Fielding H. Garrison that "even under the best of conditions, it is still possible and probable that many highly intelligent and highly educated persons will continue to hug their whims and superstitions."

In the practice of magic, "the bastard sister of science" (Frazer), man seeks to control inanimate objects and even master the processes of life by means which to him are unfamiliar and mysterious and therefore seem "supernatural."

I should like to contribute in some slight degree, to render at least somewhat familiar, the seemingly mysterious practice and results of the magic treatment of warts.

Treatment of Warts by Magic.—The employment of magic in the treatment for warts, which to this day is resorted to in every quarter of the globe by primitive as well as by civilized man so generally as to make the practice almost universal, is a familiar illustration of the persistence with which people cling to the belief or faith in the possibility of invoking so-called supernatural intervention for the relief of physical ailments.

It has been the custom to ascribe the perpetuation of these primitive attempts of healing to tradition and conservatism due to mental inertia, but no method of therapeutic procedures endures ad infinitum, unless success results from it or follows it more or less frequently. It would seem, therefore, that every physician has at least a general interest in the modus operandi of a method which, by the simple maneuver of "touching them with pebbles or muttering charms over them" (Garrison), succeeds at times in causing the disappearance of tumors which are defined by Jadassohn as infectious benign epitheliomas, and classified by Ewing and others as papillomas or acanthomas.

Directions for the Cure of Warts by Magic.—To serve as a basis for the discussion, it will be useful to describe briefly the essential features of a series of directions for the cure of warts by magic.

1. At the time of the waning moon cut criss-cross into a Borsdorfer apple; press the wart so forcibly with the cut surface of the apple that it pains severely, then bury the apple in the ground. As soon as the apple rots, the wart will disappear.

2. When the moon wanes, rub the wart with a piece of green, unsalted pork until the skin around the wart is red, then bury the piece of pork in the ground. When the pork has rotted, the warts will also decay and drop off.

3. Take a long piece of thread and tie a loop so tightly into a knot around the base of each separate wart that the thread cuts into the wart. Then bury the thread with the loop under the eaves; when the thread rots the warts will disappear.

4. In the first glow of the new moon press on each wart a pea so severely that the blood commences to ooze from around the wart. Use a different pea

for each wart. Tie the peas in a cloth and throw them behind you over your left shoulder. The warts will disappear in time.

5. Cut in half a hard apple or a raw potato and rub the wart so vigorously with the cut surface, that the wart begins to bleed. With a string tie together the cut surfaces of the apple or of the potato and bury it under the eaves or throw it into a river. As soon as the apple (potato) has rotted, the wart will disappear.

To this collection, gathered in part in Central Europe, in part from immigrants originating there, I will add the following practices which are current in North Africa:[2]

6. In the Hiaina, an individual with warts (tulan) massages them forcibly during lightning, in the belief that there is a curative power in the lightning.

7. As the faith in the healing powers of the new moon seems well nigh universal, one is not surprised to find that the Ait Sadden treat their warts by imploring the new moon: "O new moon, o new moon, take from me my warts." While this incantation is repeated, the moon is allowed to shine on the warts.

8. In Morocco the blood from the hedgehog is held to be powerful medicine and among other things also believed to be efficacious in the treatment of warts.

9. In Morocco, the specialization in the treatment of disease prevails also among the saints and one of them (Sisi Bbwarak) may be invoked for the cure of warts.

Comment.—The methods described may be divided into two groups according to whether the magic treatment results in trauma or not.

Although it is difficult to estimate with any degree of accuracy the significance of the rôle which the trauma plays in bringing about a cure of the warts, I believe for the following reason that it is at least a contributory factor in the curative process.

Until Jadassohn, Ciuffo, Variot, Lanz, de fine Licht, Wile and Kingery, Lipschütz, Wälsch and others showed that the success of inoculation experiments with warts depends on the introduction of the transplant into the epidermal layers with the avoidance of the cutaneous and subcutaneous structures, inoculation experiments had been uniformly unsuccessful. From this the conclusion is inevitable that contact with the constituents of the subepidermal strata interferes with the development of the transplant.

Since trauma of the wart may establish a contact with the deleterious tissue constituents, a curative disintegration of the wart may result from any method of treatment which produces trauma.

Methods that employ injections into the warts may, in part at least, also depend for their curative effects on the trauma that they cause.

---

2. Westermarck, E.: Ritual and Belief in Morocco, New York, Macmillan Company, 1926.

In view of certain observations to be mentioned later, it is possibly the contact with the tissue fluids, rather than with the structures themselves, that have to be looked on as the substances inimical to the warts.

But to what process is one to attribute the curative effects produced by so-called methods of magic that do not cause any visible injury to the wart or its hosts?

Since in the recent publications, especially of Bloch and of Bonjour as well as of others, the treatment of warts by suggestion has received, if I may so term it, official approbation, one is no longer condemned to ridicule for referring a cure of this physical ailment to psychic influence.

THE CURE OF WARTS BY SUGGESTION

In explanation of the mechanism of the curative processes due to suggestion, I draw attention to the familiar experiments by Wetterstrand, Jendrassik, Krafft-Ebing, Focachon, Bernheim, Kaposi, Cassirer, Beaunis, Kreibich, Kohnstamm and Pinner, Forel (reported by Moll), Maurice B. Wright, Hadfield, Walterhöfer, von Szölösy, Heller and J. H. Schultz, Alrutz, Bolten, Schindler and others, who demonstrated that nervous impulses may cause functional changes in the walls of the blood vessels permitting an extravasation of fluid and a diapedesis of erythrocytes. The alteration of the walls of the capillaries is functional in character. According to the variation in the duration and the intensity of the functional stimulus, there is a corresponding variation in the duration and amount of the extravasation.

The functional change is subject to suggestional and volitional influences and may be so localized, at least in psychopathic persons, that the extravasation takes place in predetermined regions of the body.[3]

According to Krogh:

> Certain reflexes affecting the capillaries of the skin have their reflex path over cerebral centers and are appropriately classed as psychic reactions:
>
> Everybody knows that these reactions manifest themselves through distinct and sometimes quite sudden changes in the blood color of the skin. This means that they are brought about chiefly by tonus variations in the capillaries and venules. Lewis has shown by temperature measurements that the arterioles are also involved, since the blush is accompanied by a rise in skin temperature, while the skin which has turned pale from fear or sorrow is proverbially cold.[4]

---

3. Cannon, W. B.: The Mechanism of Emotional Disturbance of Bodily Functions, New England J. Med. **198**:877, 1928. Köhler, W.: Gestalt Psychology, New York, H. Liveright, 1929. Neuburger, Joseph: Die Stigmata-Frage (Konnersreuth), Deutsche med. Wchnschr. **53**:1936, 1927. Schultz, J. H.: Stigmatisierung und Organneurose, Deutsche med. Wchnschr. **53**:1584, 1927.

4. Krogh, August: The Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1930, p. 154.

From the work of Thomas Lewis, one would expect the reaction to be due to the local production of a vasodilator substance (called H-substance by Lewis, possibly histamine).

From this array of observations, one has to conclude that in the successful cases suggestion, like trauma, may result in bringing the warts in contact with tissue constituents derived from subepidermal structures and may thus produce a cure.

As neither the treatment by magic nor the treatment by suggestion results in a cure in every case, one has to assume that contact with the wart is not established in the unsuccessful cases.

According to the foregoing explanation, the disappearance of the warts after treatment is in principle the result of a change in the host. It would manifestly strengthen the significance of this explanation if alterations in the host tissue brought about by more direct intervention would also lead to the cure of warts.

To some extent the methods of treatment to be presented next fulfil this postulate.

TREATMENT OF WARTS BY INJECTIONS OF ARSPHENAMINE

The announcement of the discovery by Japanese investigators (1921) of a spirochetal etiology of warts prompted me, like other dermatologists, to give the spirocheticidal agents κατ' ἐξοχήν, i. e., Ehrlich's arsenicals a trial in the treatment for multiple warts. The results were only moderately satisfactory with the chemical employed, neoarsphenamine. Perhaps, not more than 40 or 50 per cent of the cases responded to the drug, which was administered by intravenous injection. Nevertheless, the results were sufficiently encouraging to induce me to give sulpharsphenamine a trial, when this drug made its debut, or rather celebrated its renaissance. The fact that sulpharsphenamine can be injected intramuscularly constitutes an advantage in several respects.

In making these injections, I returned to the technic originally adopted by me for the intramuscular injection of arsphenamine to the extent that I mixed the aqueous solution of sulpharsphenamine with the patient's blood. In the case of arsphenamine this was done not only because of the opinion advanced by Ehrlich that the therapeutic effect would thereby be enhanced, but also because experience had taught me that the irritation at the site of the injection is diminished by the previous admixture of blood.

AUTOHEMOTHERAPY OF WARTS

As sulpharsphenamine proved to be superior to neoarsphenamine in its curative effects on the warts, I had intended to determine whether this superiority was due to the difference between the two chemicals,

to the addition of the blood or to the blood per se? Chance came to my aid in arriving at a decision on the efficacy of the blood. (The solution of the two other therapeutic problems was not attempted.) The chance consisted in the fortuitous omission of the addition of the sulpharsphenamine to the blood.

Comment.—As the Japanese reports of the spirochetal etiology remain unconfirmed, the curative results obtained with the arsphenamines must be attributed to the general resistance building effects developed in the host by the drug. This stimulation of the cellular defense mechanism of the body (Stokes) or the so-called activation of the protoplasm (Weichardt) is also produced by the injection of foreign protein. Notwithstanding the fact that the proteins injected in autohemotherapy are derived from the patient's blood, they are foreign in at least two respects. First, they are foreign to the structure in which they are placed by the injection. Second, the proteins of which the constituents of the injected blood consist are not absorbed until they have been broken down by enzymes produced by the adjacent cells or transported to the site of the injected blood. The products of cleavage can enter by diffusion through the vessel walls into the lymph (J. H. Lewis) and the blood stream (M. Landsberg).[5] The corpuscular elements must also be disintegrated previous to their absorption.

It would be interesting to investigate whether injections of autogenous and heterogenous serums; of suspensions of the cellular elements of the blood of the patient, and of others produce analogous results.

I have sought to obtain blood from those who do not have and never have had warts, but I have found it difficult to find persons who fulfil the latter requirement. Perhaps absolute and permanent absence of warts need not be insisted on, because a lasting immunity seemingly does not develop in patients with warts.

In one instance in which the opportunity presented itself to practice heterohomohemotherapy, it proved successful as to therapeutic result and uneventful as to disturbing side effects, such as anaphylactic shock, serum disease, etc. The donor formerly had warts.

It is manifestly not within the scope of this discussion to take up the consideration of the various aspects of foreign protein therapy. I agree with Sahli that such terms as "protoplasma activation" are little else than slogans or catchwords, but so far as the problem under discussion in this paper is concerned, it does not matter what epigram is employed to designate the fact that an injection of the patient's blood in many cases causes the disappearance of his warts.

---

5. Krogh (footnote 4, p. 365).

If one were to maintain in explanation of the curative effects of blood injections on warts that autohemotherapy is nothing but suggestion therapy, it might be said that in that case all foreign protein therapy must be looked on as suggestion therapy unless the treatment for warts constitutes the proverbial exception to the rule.

I would prefer to reverse the argument and say that suggestion therapy accompanied by extravasation of blood or serum is a form of foreign protein therapy. This reasoning is not a juggling of words or a transposition of terms, because, although physicians differ as to the explanation of its mechanism, they all preach and practice foreign protein therapy in one form or another, whereas suggestion therapy is not and perhaps never will be practiced successfully by the majority.

At all events, I feel that I am not transgressing the limits of probability, when I assert (1) that an alteration was produced in the host's body by direct therapeutic intervention, and (2) that the disappearance of the warts followed the injection and the ensuing alteration. These observations may also be applied to a tentative explanation of the spontaneous disappearance of warts.

SPONTANEOUS DISAPPEARANCE OF WARTS

If the explanation seems plausible that the disappearance of warts following the treatment by magic, by suggestion or by injection of the patient's blood results from a change in the host of the warts, it seems logical to infer that the so-called spontaneous disappearance may also be due to the same cause, i. e., to an alteration of the soil on which the virus is implanted.

In answer to the question how such a change in the host may arise, I suggest that this might come about through accidental or intentional, enforced or voluntary, omissions of certain food constituents from the diet. Likewise it is necessary to reckon with additions to the diet.

Experimental observations on some of the numerous diseases of plants due to infection or infestation with parasites (bacteria, viruses, fungi, etc.) have shown that changes in the vigor of the host due to change in the chemical composition of the soil or due to prolonged variation in the temperature or in the moisture of the atmosphere affect the parasite favorably or unfavorably. The recent revival of the therapeutic endeavors to influence bacillary infections through modifications of the diet may also be cited in support of the view that a change in the soil may affect an infectious agent and its activity. Although the therapeutic results in the other forms of tuberculosis are not conspicuously favorable, in the cutaneous form, especially in lupus vulgaris, the diets of Gerson and of the Herrmannsdorfers have been credited with success by several clinicians. Dietary experiments

for the observation of their influence on such trivial conditions as warts would not be justified ordinarily, but this influence might be noted in patients who are on a diet for more serious conditions.

The spontaneous disappearance of warts may be the result of a number of other causes originating in the host.

The host may produce at some time or other sufficient antibodies [4] or other chemical agents to overcome the invader; in other words, the host's resistance may increase. Again the host may fail to furnish the proper kinds and amounts of nutrients for the normal development of an active virus; in other words, the resistance of the virus may decrease. Inadequate nutrition of the host may also interfere with the growth of the wart, which may shrink, if not entirely disappear. Localized accumulation of its own products of metabolism may destroy the virus or at least reduce its resistance sufficiently to enable the host to cope with it successfully.

INDIRECT EFFECTS OF IRRADIATION ON WARTS

That a number of nonirradiated warts may disappear at the same time as irradiated ones is a phenomenon that is frequently observed. The irradiated warts disappear owing to the chemical decomposition produced by the impinging rays, which are selectively absorbed.

The mode of action of the rays is most satisfactorily explained by the application of "The Quantum Theory in Biology," as developed by Schneider and Sperti and their collaborators in the publications of the Institute of Scientific and Industrial Research, University of Cincinnati. One may compare the action of the rays to the selective action of Ehrlich's organotropic or etiotropic chemical compounds.

In explanation of the indirect effects of radiation, several hypotheses may be advanced. According to one, the tele-effect is the result of the reaction produced by the destruction of the cellular elements in the warts that were irradiated. The secondary therapeutic action, accordingly, may again be attributed to the foreign proteins that enter the circulation. Another hypothesis assumes that the virus is disintegrated by the radiation; the liberated toxins give rise to a production of antibodies which the lymph and the blood currents transport to the untreated warts, where a focal reaction ensues which may destroy the warts. It seems probable that both factors act synergistically in the production of the therapeutic results.

RELAPSES

When injections are employed, I, like other observers, have noted now and then that after treatment a group of warts flattened out or "subsided" as it were, but did not go on to complete disappearance. Instead of continuing the process of regression, the warts commenced

to grow again in situ, and in a short time were as large as before treatment. In several patients this alternate subsidence and recrudescence occurred repeatedly before the warts succumbed to the treatment. One patient, at least, did not continue treatment until a cure could be accomplished. Several times a change of treatment was necessary to effect a cure. It would seem that in these relapsing cases a part of the virus escapes complete annihilation and develops a specific or general resistance to treatment.

THE ACTION OF VARIOUS DRUGS

Arsenic and Mercury.—The therapeutic effects on warts of the inorganic compounds of these two metals are to be ascribed to the changes in the capillaries which parallel those of inflammation. The capillaries are relaxed, or after large doses are paralyzed. Their permeabilty is increased which results in a tendency to exudation into the connective tissues. Extravasation of the corpuscular elements of the blood may occur.

The rapidity and the degree with which these changes develop in the host vary greatly in different persons because, speaking with Jadassohn: "Der Reiz ist nichts, die Disposition alles." ("The stimulus is nothing, the disposition everything.") The therapeutic result varies correspondingly, as one knows from experience.

Arsphenamines.—Here too the patient's disposition to react to the drug varies widely. The active hyperemias that are observed in some persons resemble the psychic erythemas discussed before. Here again, one may apply Jadassohn's dictum to explain the differences in therapeutic efficacy. Perhaps they are due to quantitative variations in the production and liberation of the H-substance of Thomas Lewis.

Magnesium Sulphate.—In attempting to explain the therapeutic effects of magnesium salts on warts, I have to venture on the thin ice of speculation. In principle, one can attribute the effect to an antagonistic action of the magnesium ion to the calcium ion. Calcium salts diminish the permeability of the vessel walls; if this action is counteracted by magnesium, the permeability is increased and one can expect the results presented repeatedly in this paper. The pharmacologic antagonism of magnesium to calcium may be augmented by the removal of some of the calcium by precipitation as sulphate. This removal increases the preponderance of the magnesium. However, only the noncolloidal calcium is precipitable by the sulphate. But the two forms of calcium, the colloidal and the ionized, are in dynamic equilibrium. The supply of one form is replenished from the other. But long continued treatment with magnesium sulphate may eventually lead to a diminution of the total supply of available calcium. (If other magnesium compounds are used, the last factor does not come into play.)

The speculative element in this explanation is principally the question of dosage. Can the small amounts of magnesium prescribed exert an appreciable therapeutic influence or does one again have to depend for the explanation on suggestion as the curative element in the treatment with magnesium compounds?

PRINCIPLES REGULATING THE REACTIONS IN TREATED WARTS

In the foregoing discussions and explanations I have employed largely the somewhat allegoric or parabolic terminology borrowed from philosophy, which has proved so valuable heuristically, but which is challenged by some authors because of the underlying teleologic implications and inferences.

I shall therefore consider the problem from another standpoint.

Frequently an untreated wart seems to persist for some time without undergoing an appreciable increase or diminution in size.

Biophysically and biochemically speaking, such a wart is in a state of equilibrium with its environment. But this equilibrium is not stable, it is dynamic; anabolism and katabolism do not cease; they equal one another. Coordination is maintained in the multicellular wart, if one may look on it as an individual organism, in conformance with Frédéricq's extension of the principle of Le Chatelier. According to this principle, "the living organism is such that each disturbing influence produces in the organism itself a compensatory reaction which tends to neutralise the disturbance and restore the equilibrium."

This is a principle that governs the posttherapeutic reactions in the wart.

Therapeutic interventions are the influences that disturb the wart organism and evoke in the wart a compensatory reaction which tends to overcome the disturbance and restore the equilibrium. It is evident that if therapy results in a cure, the compensatory reaction of the wart did not suffice to neutralize the therapeutic disturbance. If, on the contrary, the compensatory reaction of the wart suffices, the tumor starts to grow again notwithstanding the therapeutic efforts.

This explanation does not ascribe the posttherapeutic reactions taking place in the wart to a struggle between a hostile invader and its anthropocentric human host. It is silent on the teleologic aspects of the effects of treatment; it offers no comment on the usefulness of a cure to the host or on its disastrous consequences for the virus.

An explanation based on ordinary physical and chemical principles is in the case of warts to be preferred also, because, judging from the following passage, at least one pathologist does not seem convinced that an animate invader is the cause of warts.

Ewing,[6] in his treatise on "Neoplastic Diseases," wrote:

> There are numerous clinical observations suggesting the contagiousness of warts, but on analysis they can be dismissed as examples of the transfer of peculiar chemical irritants, or exposure to the same irritant, or the actual transfer of proliferating epithelial cells.

In view of Leale's "Use of Common Warts of the Hand in Skin-Grafting," [7] which Ewing mentioned without comment, one can understand Ewing's skepticism, which, as I know from oral communications, is shared by other pathologists.

As the conditions in the transplantation by Leale and in the inoculation experiments differ considerably from each other, the conclusions based on the results of the two procedures should perhaps not be compared.

Leale's success does not seem to have been repeated by others, so far as I could find in the literature available to me. Leale's success is all the more noteworthy, in view of the not infrequent failures with skin grafts experienced by surgeons.

SUMMARY

As this paper itself constitutes a summary, I confine myself to a restatement of some of the salient observations.

1. As the methods of magic treatment for warts are identical in principle with the methods of treatment by suggestion, their results are also identical.

2. Magic treatment fortifies and supplements "suggestion" by employing mechanical manipulations causing trauma, which alone may cause the disappearance of warts.

3. Autohemotherapy is useful in the treatment for warts, even though it is not uniformly successful.

4. The disappearance of warts following the treatment by magic, by suggestion, by injection of the patient's blood or of foreign protein derived from other sources, as well as the so-called spontaneous disappearance of warts, are causatively linked with a change in the host of the warts.

5. Unless the host overcomes all the invaders, the warts return sooner or later.

6. In the treatment of warts, I can rule out (using Bacon's definition) "Instances of Magic . . . by which I mean those wherein the

6. Ewing, James: Neoplastic Diseases, ed 3, Philadelphia, W. B. Saunders Company, 1928.

7. Leale, Charles A.: Use of Common Warts of the Hands in Skin Grafting. Med. Rec. **14**:188, 1878.

material or efficient cause is scanty and small as compared with the work or effect produced; so that even when they are common, they seem like miracles, some at first sight, others even after attentive consideration."

7. Although so far "we do not find ourselves possessed . . . of the laws which govern the behaviour of protoplasm under physiologic and pathologic circumstances" (Martin H. Fischer), I have tentatively applied to the hygiogenic processes occurring in warts after treatment the principle of Le Chatelier and Frédéricq in the hope of reducing by one "the number of phenomena which some are still content to explain as due to a mysterious vital action instead of simply confessing that they are yet not understood" (D. Noël Paton).

ABSTRACT OF DISCUSSION

DR. HOWARD FOX, New York: Dr. Zwick, in his discussion of this fascinating subject, mentions several theories as to how the roentgen rays may act in causing the disappearance of warts. Since the astonishing publication of Bloch, who was able to cure approximately 50 per cent of common warts and 80 per cent of flat warts by suggestion, I have been wondering whether the results we get from radiotherapy may not also be due in large measure to the power of suggestion.

DR. WALTER J. HIGHMAN, New York: I find this paper of Dr. Zwick's fascinating for, without having realized the significance of one or two of my experiences, I do now, in the light of the recent developments in the treatment of warts by means not ordinarily subscribed to by physicians. A few years ago I had a young patient, an actress, whose face was literally studded with juvenile warts that had been resistant to all therapeutic methods. Finally, on a certain Thursday, I suggested that on the next Tuesday I would start treatment with radium. She came the next Tuesday with her face just as clear as a baby's. She said she had gone to bed the intervening Saturday night with her face covered with warts, and when she awakened the next morning they had entirely disappeared. I imagined that since such warts are infections that there had been a crisis, in the sense of pneumonia, which I suppose is no more ridiculous than many other views.

In another case, a child of 7, in whom I removed the warts by fulguration, with prompt recurrence, I followed with roentgenotherapy as a mild placebo, and within twenty-four hours thereafter the warts were gone. The roentgen rays cannot do this in twenty-four hours.

In connection with the main burden of Dr. Zwick's paper, it may interest you to read Seabrook's book entitled "Jungle Ways." He made an intensive study of magic in Africa. The medicine men are not fooling themselves any more than they are us, but they furnish us a field for study of the bearing of so-called inorganic phenomena on so-called organic ones. It is simpler to ridicule what we do not understand than to make the effort to discover if such ridicule is justified.

DR. JOSEPH GRINDON, St. Louis: I wish to record a personal experience. Some years ago I noticed that I had a wart next to my thumb nail. Being busy with various things every day, I put off doing anything about it. At that time

I was destroying warts by electrolysis, and finally decided that it was disgraceful for a dermatologist to go around with a wart on his hand in plain sight. I decided I would destroy it the next morning without fail. I did not do so, but about three days later I got everything ready and on looking for the wart found it had disappeared. I could not discover the place where it had been. I have never since been able to remember on which thumb the wart was. I cannot speak in terms of Tuesdays and Thursdays, but there was an interval of perhaps three days between my last observation of the wart and its disappearance. I think the next time I see a patient with warts I will advise the time-honored treatment of burying a toad in the waning of the moon.

DR. JOSEPH V. KLAUDER, Philadelphia: In laboratory and clinical investigation, the matter of control studies is of great importance. In well conducted laboratory investigation, control study is nearly always possible, whereas in clinical investigation, such study is not always possible, or is frequently not considered. Conclusion based on clinical investigation is frequently post hoc. Conclusion of the effect of a therapeutic agent should always be considered in the light of the course of the disease, in the absence of that therapeutic agent. Applying this principle to the effect of suggestion in the treatment for warts, it is to be noted that warts, in the absence of any treatment, spontaneously disappear. Therefore, how valid is the conclusion that suggestion is a means of causing warts to disappear? In view of this consideration, I hesitate to draw conclusion as to the therapeutic efficacy of suggestion since it is impossible to know if the wart would have spontaneously disappeared if suggestion had not been employed. If any conclusion is to be drawn, it would be desirable to know the percentage of all warts that disappear spontaneously and the percentage that disappear following suggestion.

DR. FRED D. WEIDMAN, Philadelphia: We have passed from the actress down to Dr. Grindon, and now I wish to bring up a mule. When I was a student, our professor of pathology used to tell us about a mule on his farm. Professor Allen J. Smith was one of the most scientific and best informed men I have ever known, a true scientist. He told us that he had consulted first class veterinarians and obtained their advice in regard to this mule, who had a tumor of some kind on his leg. Nothing had any effect therapeutically, and finally his farm hand suggested that they have a gypsy come and pow-wow. Dr. Smith agreed to this, and within forty-eight hours the large lump disappeared from the leg of the mule.

DR. KARL G. ZWICK, Cincinnati: Although I would deplore the circumstance, if a more than passing attitude of jocundity should result from my reference to it, I feel under obligation to Dr. Stillians for privately drawing attention to my omission from the pertinent literature of that classic chef d'oeuvre of American humor, "The Adventures of Tom Sawyer," in which the author refers not only to magic methods for the cure of warts, but also to certain factors active in their etiology.

In connection with Dr. Klauder's remarks, I can only say that I shared his opinion at one time.

The cure of warts by suggestion was (many years ago) first brought to my notice when I had occasion to observe the almost uniform success attained with this method by the celebrated Swiss geologist Heim. Heim's success was useful to him, because by it the Swiss peasants were induced to assist him in various ways (gifts of minerals, service as guides) in his work. The interest of Bloch, of Zürich, was also aroused by Heim's success. Bonjour, of Lausanne, a well known neurologist, has published several important contributions in which he

reports a number of successful treatments by mail. Bloch and Bonjour were the first, I believe, to tabulate their successes and failures statistically.

Those of us who fail to achieve success with suggestion therapy can at least console ourselves that we are in first class company, as both Jadassohns, pater filiusque, (according to a personal communication) are also only occasionally successful.

In closing I may restate that for me the cardinal purpose of this study was the formulation of some distinct concept, a working hypothesis if you will, of the seemingly mysterious behavior of warts. Such a concept ought to reflect and test the tenets of our "Weltanschauung," our philosophy of life!

For instance, do we believe in the causality principle? Do we hold with the majority of educated persons, although in opposition to some of the neophysicists, that nothing happens without there being an adequate cause? Or do we believe, with the superstitious savage, the untutored individual, in magic?

LX.—THE EFFECT OF THALLIUM ACETATE ON THYROIDECTOMIZED ALBINO RATS*

ZOLA K. COOPER, PH.D.
ST. LOUIS

In recent years the use of thallium acetate as a depilatory in cases of ringworm of the scalp has focused considerable attention on this drug. Clinically, a single dose of 0.008 Gm. of thallium acetate per kilogram of body weight given by mouth is sufficient to cause the hair of the scalp to fall. The drug can be used with safety only in children who have not yet reached the age of puberty. The question of how the drug acts within the body in order to produce its characteristic effect on the hair is still unsettled. Four theories have been proposed to explain its action: (1) that thallium acts directly on the hair follicle; (2) that the drug affects primarily the central nervous system, and that the effects on the hair are secondary; (3) that thallium affects the sympathetic nervous system and through it the hair; (4) that thallium directly affects the endocrine system and indirectly the hair. (Some workers combine the latter two hypotheses and consider that thallium acts through the endocrine-sympathetic system.)

Of these four theories, that which seeks to explain the action of thallium by its effects on the endocrine organs is perhaps the most widely held. In a long series of papers Buschke and his associates [1] have shown that the testis, the ovaries, the hypophysis, the adrenals, the parathyroids and the thyroid, individually or collectively, may be affected in animals to which thallium has been administered.

Recently considerable attention has been focused on the rôle of the thyroid gland, in particular, in producing the effects that follow the administration of thallium acetate to experimental animals. Buschke observed an atrophy of the follicles of the thyroid and a flattening of the epithelium after the administration of thallium. He did not stress

---

* Submitted for publication, Nov. 23, 1931.

* This work has been financed by an anonymous grant to the Dermatological Department of Washington University for the study of hair.

* Studies, observations and reports from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., service of Dr. M. F. Engman and Dr. W. H. Mook.

1. Buschke, A., and Peiser, B.: Dell'azione biologica dell'acetato di tallio, Gior. ital. di dermat. e sif. **70**:585 (June) 1929; abstr., Arch. Dermat. & Syph. **20**:524 (Oct.) 1929.

the importance of the changes in this gland, however, since, as has been mentioned, he also found equally important evidence of changes in other endocrine organs. Pardo-Castello,[2] however, stated that "the fall of hair caused by the administration of thallium acetate is due to thyroid dysfunction, which causes a partial syndrome of thyroid insufficiency." This opinion is based on experiments with a relatively small number of guinea-pigs and cats, most of which received lethal doses of thallium acetate. At autopsy the thyroids in some of these animals were found to be small and "lost in the surrounding connective tissue." Microscopic study of sections of these glands showed atrophy and parenchymatous degeneration.

Leigheb [3] also found alterations of the endocrine glands, "sufficiently marked to warrant the opinion that the alopecic properties of thallium depend on the action of this drug on the ductless glands." Of these glands, the thyroid seemed to be the most affected.

Mu and Hu [4] have made a study of the effect of injections of thallium acetate on the basal metabolism of rats. Doses of 0.008 and 0.012 Gm. of thallium acetate per kilogram of body weight caused a definite but transitory diminution of the basal metabolic rates between the second and eleventh weeks after the administration of the drug. The diminution was more marked and more persistent following the use of the larger dose. During the time of the depression of the basal metabolic rate, the animals became inactive and their hair fell, particularly when their metabolism was at its lowest level.

Ma and Mu [5] found that a single injection of 0.008 Gm. of thallium acetate per kilogram of body weight into a rat produced definite changes in the mitochondria and Golgi apparatus of the cells of the thyroid gland. The Golgi apparatus became changed from network into droplets, the mitochondria from filaments into segmented granules that were dispersed in the distal portions of the cells. The thyroid cells became "definitely flattened," and their nuclei stained poorly. The staining properties of the colloid substance changed from basophilic to acidophilic. Six weeks after the injection complete recovery of all the cellular structures was observed. The authors attributed these morphologic changes, together

2. Pardo-Castello, V.; Mestre, J. J., and Rio, E.: Tinea of the Scalp, Arch. Dermat. & Syph. **19**:409 (March) 1929.

3. Leigheb, V.: Ricerche sperimentali sulla intossicazione da tallio, Gior. ital. di dermat. e sif. **69**:960 (June) 1928; abstr., Arch. Dermat. & Syph. **19**:295 (Feb.) 1929.

4. Mu, J. W., and Hu, C.: Effect of Thallium Acetate on the Basal Metabolism of Rats, Proc. Soc. Exper. Biol. & Med. **27**:251 (Jan.) 1930.

5. Ma, W. C., and Mu, J. W.: Cytological Changes in Thyroid Apparatus and Spinal Ganglia of Rats Treated with Thallium, Proc. Soc. Exper. Biol. & Med. **27**:249 (Jan.) 1930.

with the transitory diminution in the basal metabolic rate, demonstrated by their colleagues, to the direct action of thallium on the thyroid gland.

With these results in mind the present study of the effect of thallium acetate on thyroidectomized rats was undertaken in an attempt to determine further the relation of the thyroid to the action of thallium acetate.

MATERIALS AND METHODS

The thyroid gland was removed from a series of twenty-eight albino rats. The superior and inferior thyroid vessels were ligated, and both lobes and the isthmus of the gland were extirpated. The parathyroid glands, which are two in number in the rat and are embedded in the ventral surface of the thyroid, were left intact with as little thyroid tissue as possible surrounding them. On the death of the animal, an autopsy was performed in every case, and in no case was regeneration of the thyroid found.

A control group of twenty-seven normal rats was used. In each case care was taken to select a control animal of the same sex and of approximately the same age and weight as the thyroidectomized animal with which it was to be compared.

To both the thyroidectomized and the normal animals sublethal and lethal doses of thallium acetate were administered. The rat can tolerate larger doses of thallium acetate than most other species, many rats suviving doses of 0.018 Gm. of thallium acetate per kilogram of body weight and even larger doses. After the administration of such doses, the coats of the animals usually became roughened and a general falling of the hair over the entire body followed. The animals in this experiment were divided into four groups that received, respectively, 0.018, 0.020, 0.026 and 0.030 Gm. of thallium acetate (Merck) per kilogram of body weight. The doses of thallium acetate for each animal were carefully weighed, dissolved in 0.5 cc. of distilled water and injected intraperitoneally. No injections of thallium acetate were given to the thyroidectomized animals until a period of about two weeks had elapsed after the operation. This would appear to be ample time for recuperation from the operation, since even on the following day the animals are active and eat normally.

The length of the period of survival following the administration of these heavy doses of thallium acetate was taken as a measure of the resistance of the animal to the drug. Autopsies were performed on all animals in order to make sure that death was due to thallium poisoning.

EXPERIMENTAL WORK

The thyroid glands were removed from ten adult rats (five males and five females), and after allowing two weeks or more for the animals to recover from the operation, they were given injections of 0.018 Gm. of thallium acetate per kilogram of body weight. Nine normal animals (five males and four females) were also given injections of 0.018 Gm. of thallium acetate per kilogram of body weight. It has been found in previous work that many rats can withstand a dose of 0.018 Gm. of thallium acetate per kilogram of body weight, hence the length of the survival period of the individual rat is taken as a measure of its resistance to the effects of the drug. The accompanying table shows that in

four of the cases compared the control and the thyroidectomized animal survived an exactly equal length of time. In one case the animal from which the thyroid had been removed and its control both recovered from the thallium poisoning and died after long intervals of other causes. In the three remaining cases the differences in the lengths of the survival periods of the control and the thyroidectomized animal are

Period of Survival in Days of Thyroidectomized and Control Rats Following the Administration of Various Doses of Thallium Acetate

Thyroidectomized Rats					Control Rats				
Sex	Weight of Rat in Grams	Dose of Thallium Acetate Received in Gm. per Kg.	Grams of Thallium Acetate Received	Days of Survival	Sex	Weight of Rat in Grams	Dose of Thallium Acetate Received in Gm. per Kg.	Grams of Thallium Acetate Received	Days of Survival
♂	99.7	0.018	0.0018	..*	♂	83.0	0.018	0.0015	..*
♂	101.4	0.018	0.0018	11	♂	94.1	0.018	0.0017	27
♀	169.6	0.018	0.0031	5	♀	163.5	0.018	0.0029	7
♀	156.8	0.018	0.0028	4					
♀	168.1	0.018	0.0028	4	♀	167.3	0.018	0.0028	4
♂	208.8	0.018	0.0037	4	♂	198.9	0.018	0.0035	4
♀	147.6	0.018	0.0028	4	♀	177.0	0.018	0.0033	4
♂	117.7	0.018	0.0021	36	♂	125.0	0.018	0.0023	30
♂	167.9	0.018	0.0028	9	♂	151.1	0.018	0.0027	9
Average survival period in days....				9.6	Average survival period in days....				12.1
♂	158.5	0.020	0.0031	7	♂	150.1	0.020	0.0030	..*
♂	121.5	0.020	0.0024	12	♂	101.0	0.020	0.0020	17
♂	127.6	0.020	0.0028	5	♂	135.0	0.020	0.0029	5
♂	107.7	0.020	0.0021	12	♂	128.3	0.020	0.0025	5
♂	192.0	0.020	0.0038	6	♂	161.0	0.020	0.0032	6
Average survival period in days....				8.4	Average survival period in days....				8.2
♂	200.0	0.026	0.0053	2	♂	149.8	0.026	0.0040	1
♂	146.0	0.026	0.0038	6	♂	150.6	0.026	0.0040	6
♀	161.9	0.026	0.0043	6	♀	137.6	0.026	0.0036	..*
♀	158.0	0.026	0.0041	..*	♀	139.1	0.026	0.0036	..*
♂	166.9	0.030	0.0050	5	♂	197.0	0.030	0.0059	3
♂	181.0	0.030	0.0054	..*	♂	178.3	0.030	0.0053	4
♂	162.2	0.030	0.0048	7	♂	141.0	0.030	0.0042	3
♂	193.6	0.030	0.0058	3	♂	211.6	0.030	0.0063	3
♂	138.4	0.030	0.0041	6	♂	175.0	0.030	0.0052	5
♀	145.3	0.030	0.0043	5	♀	150.7	0.030	0.0045	3
♀	166.3	0.030	0.0049	3	♀	150.0	0.030	0.0045	3
♀	151.1	0.030	0.0045	8	♀	172.7	0.030	0.0051	6
♂	134.2	0.030	0.0040	5	♂	135.6	0.030	0.0040	5
♂	135.0	0.030	0.0040	6	♂	134.3	0.030	0.0040	3
Average survival period in days....				5.3	Average survival period in days....				3.8

* These animals survived for a period of months and died of causes other than thallium poisoning.

not great. In one case the animal deprived of its thyroid outlived its control; in two other cases the controls lived somewhat the longer. Excluding the two rats (one control and one thyroidectomized animal) that did not succumb to thallium poisoning but lived for a long period and died of other causes, the average survival period of the controls (12.1 days) is somewhat longer than that of the thyroidectomized animals (9.6 days).

The thyroids were removed from a second smaller group of animals, comprising five males. After a two week period for recuperation, each

of these animals received by intraperitoneal injection 0.020 Gm. of thallium acetate per kilogram of body weight. Five control males received similar doses of thallium acetate. The table shows that all the rats in this group, both control and thyroidectomized, succumbed to thallium poisoning with the exception of one control. In two cases the controls and the thyroidectomized animals succumbed in exactly the same length of time. In one case the thyroidectomized rat survived seven days longer than did its control, while in another case the control outlived for five days the animal deprived of its thyroid. The average length of the survival period for the thyroidectomized rats was 8.4 days; that for the control rats was 8.2 days.

A third group of four thyroidectomized and four control animals received intraperitoneal injections of 0.026 Gm. of thallium acetate per kilogram of body weight. Of these, one animal deprived of its thyroid and two control animals did not succumb to thallium poisoning. In one of the remaining two sets of rats compared, the survival periods of the control and thyroidectomized animals were equal; in the other, the thyroidectomized animal outlived its control by one day.

The thyroids were removed from ten rats, and after allowing the usual period for recovery, these animals received intraperitoneal injections of 0.030 Gm. of thallium acetate per kilogram of body weight. Ten control rats received the same dose of thallium acetate by intraperitoneal injection. Of this group of animals all but one, a thyroidectomized male, died within a short period from the effects of thallium. In three of the pairs compared, the control and the animal on which the operation had been performed lived for the same number of days after the injection of thallium acetate. In the remaining seven sets the thyroidectomized animals remained alive somewhat longer than did the controls. The average survival period for the thyroidectomized animals was 5.3 days; that for the control animals was 3.8 days.

In some of the animals sufficient time elapsed before death for changes in the coats to appear. No differences could be noted in the degree to which the hair was affected in control and thyroidectomized animals.

COMMENT

From these results it would seem that removal of the thyroid gland has little, if any, effect on the reaction of the rat to thallium acetate. Taking the experiment as a whole, the number of control and of thyroidectomized animals succumbing to the administration of these relatively large doses of thallium acetate were remarkably close (twenty-five thyroidectomized animals and twenty-three controls). Moreover, the lengths of the survival periods of the control and experimental animals in all the four groups treated are strikingly similar. Although

the average survival period of the controls is slightly longer than that of the treated in the first group, receiving 0.018 Gm. of thallium acetate per kilogram of body weight, conditions are reversed in the last group, receiving 0.030 Gm. of the drug per kilogram of body weight, in which the average survival period of the experimental animals is greater than that of the controls. In the smaller second and third groups, receiving 0.020 and 0.026 Gm. of thallium acetate per kilogram, the survival periods of control and thyroidectomized animals are even nearer the same duration than in the other two groups.

Moreover, no gross differences could be observed in the degree to which the coats of experimental and control animals were affected by the administration of the thallium.

These results seem to indicate that perhaps the thyroid gland does not play so important a rôle in the reaction of the organism to thallium acetate as has been previously supposed since the reactions to the drug are not different in animals with thyroids removed than in those with thyroids intact. The changes, described by other workers, in the thyroid glands of animals to which thallium had been administered may have been secondary rather than primary.

SPOROTRICHOSIS

WITH REPORT OF A RATHER UNUSUAL CASE

LOUIS B. MOUNT, M.D.

ALBANY, N. Y.

In the *Bulletin of the Johns Hopkins Hospital* of December, 1898, there appeared an article entitled "On Refractory Subcutaneous Abscesses Caused by a Fungus Possibly Related to the Sporotrichia," by B. R. Schenck. The primary point of infection was on the index finger, whence it extended up the radial side of the arm, following the lymph channels and giving rise to several circumscribed indurations that were in part broken down and ulcerated. From this case an organism was recovered twice in pure culture and classified by E. F. Smith of the United States Department of Agriculture as belonging to the genus Sporotrichum created by Link in 1809. Almost one hundred years had elapsed from the time the genus was created until proof was obtained of the pathogenicity of one of its species for man.

Schenck carried out a problem in research in a scholarly fashion. He carefully described the cultural characteristics, the morphology and the development of the organism, together with the results of experimental inoculation into animals.

Great credit is due Schenck, for as a result of his research there was added to dermatology the description of a disease worked out completely in the United States.

Soon similar cases were portrayed by Brayton, in 1899,[1] Hektoen and Perkins,[2] in 1900, and Quain,[3] in 1904. Hektoen gave the name Sporotrichum schenckii to the fungus.

From this time on, the disease was seemingly forgotten, in North America at least, until the publication of Duque's[4] article in 1908. Rareness of the disease certainly cannot be cited as the cause for the lack of reports in American journals. It must have been due either to the nonrecognition of the disease or to an indifference in the matter of recording cases. As a marked contrast to this, the striking rapidity of such reports following the publication of de Beurmann's[5] article in 1903 in France should be noted.

---

* Submitted for publication, Feb. 8, 1931.

* Read at the Fifty-Fourth Annual Meeting of the American Dermatological Association in June, 1931, at Toronto, Canada.

1. Brayton: Indianapolis M. J. **18**:272, 1899.
2. Hektoen and Perkins: J. Exper. Med. **5**:77, 1900.
3. Quain: St. Paul M. J. **6**:615, 1904.
4. Duque: Am. J. Dermat. & Genito-Urin. Dis. **12**:240, 1908.
5. de Beurmann: Ann. de dermat. et syph. **4**:678, 1903.

Interest in the disease seems to have been renewed in America in 1909 and 1910, with the discovery of cases among men and horses by Burlew,[6] Trimble and Shaw,[7] Pusey,[8] Page, Frothingham and Paige,[9] Sutton,[10] Stelwagon[11] and Hyde and Davis,[12] the latter two giving a masterful essay on the relationship of the disease to mycotic lymphangitis in horses. This article was read before the thirty-fourth annual meeting of the American Dermatological Society and brought forth an interesting discussion.

Sporotrichosis may be defined as a mycosis caused by a parasite, Sporotrichum, a hyphomycete, recognized by rather delicate, branching, septate threads bearing conidia or external spores. These spores, round, oval or pear-shaped, are either pedunculated or sessile, and may be scanty or numerous. When numerous, they may form a sort of sheath around the thread or may be collected at one end in a bunch.

Many varieties of Sporotrichum have been identified, at least 100, but of this large number comparatively few are thus far known to be pathogenic to man and animals. In 1926, Benedek[13] reported a case of dermo-epidermitis caused by a new species of parasitic fungus termed Sporotrichum lipsiense, the latest to be added to the causative list.

Considerable discussion has been voiced as to the similarity or difference between the variety described by de Beurmann and the one isolated by Schenck. The consensus of authorities is that the two are identical and should bear the name of Schenck because of the priority of discovery.

The natural habitat of the Sporotricha is widespread. They are found in all parts of the world and in all climates, on vegetables, grasses, bark, flowers, wild plants, thorns and grain stalks. There must be a greater prevalence in certain sections, because of the preponderance of cases reported from these districts, such as the Missouri basin in the United States.

The inoculation of a slight abrasion or wound with some infected material is the usual cause of the disease in man. Other modes of infection must exist. It is not beyond the realm of reason to believe that the fungus may make its entry through the hair follicles and through

---

6. Burlew: South. California Pract. **24**:1, 1909.
7. Trimble and Shaw: J. Kansas M. Soc. **9**:305, 1909.
8. Pusey, in discussion of Hyde and Davis: J. Cutan. Dis. **28**:352, 1910.
9. Page, C. G.; Frothingham, L., and Paige, J. B.: J. M. Research **23**:137, 1910.
10. Sutton, R. L.: Sporotrichosis, J. A. M. A. **55**:1000 (Sept. 17) 1910.
11. Stelwagon: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1910, p. 1119.
12. Hyde and Davis: J. Cutan. Dis. **28**:321, 1910.
13. Benedek: Dermat. Wchnschr. **83**:1695, 1926.

unbroken mucous membrane. In 1922, Jessner,[14] by rubbing the spores of Sporotrichum into the shaved skin of rats produced groups of small papules, but no generalized lesions. Following the same technic as Jessner, Kesten and Martenstein[15] demonstrated Sporotricha in the regional inguinal lymph nodes by the twelfth day after infection. Davis[16] has shown that Sporotrichum may pass through the intact intestinal mucosa, the migratory phagocytes being the carriers. Animals, by means of their skin, hair, mouth, etc., act as passive bearers of fungi. A great similarity exists between the rôle of these passive carriers and that played by insects in the transference of other diseases. Meyer[17] observed that ordinary house flies, having fed on the sporotrichotic organs of a rat, could infect Sabouraud's plates with the spores of Sporothrix three days after contact with the infected material, and that after death the spores remained alive on the cadavers for more than twenty days. This may be of great import because of the work of Davis cited.

There can be no doubt that man is another passive carrier, for the organism has been found in the pharynx as a saprophyte; furthermore, there is recorded an instance of the disease having been caused by the saliva of a carrier inoculating a wound. Other undoubted sources of infection are the bites of various animals and the care or handling of infected ones.

As the sporotrichotic lesion is a chronic granuloma, the histopathology reveals the changes found in such a condition. These might be termed syphiloid, tuberculoid and ecthymatous. The syphiloid changes are in the periphery of the lesion and consist of an acute inflammatory reaction of the connective tissue with vascular dilatation and an infiltration of plasma cells, fibroblasts, lymphocytes and mast cells. The tuberculoid response is in the midportion, showing large epithelioid cells and foreign body giant cells, not unlike tubercles in their arrangement. In the tuberculoid area are macrophages, erythrocytes, eosinophils and polymorphonuclear neutrophils with the formation of miliary abscesses, all making up the ecthymatous zone.

The statement made by de Beurmann and others that mycelium cannot be found in sections of sporotrichotic tissue, except in experimental lesions in the rat, is almost universally accepted, but must be challenged. In 1911, McDonagh demonstrated mycelium in sections

---

14. Jessner, M.: Klin. Wchnschr. **1**:2428, 1922.

15. Kesten, Beatrice, and Martenstein, Hans: Experimental Sporotrichosis, Arch. Dermat. & Syph. **20**:441 (Oct.) 1929.

16. Davis: J. Infect. Dis. **19**:688, 1916.

17. Meyer, K. F.: The Relation of Animal to Human Sporotrichosis, J. A. M. A. **65**:579 (Aug. 14) 1915.

of a lesion obtained from Adamson's [18] case. Forbus [19] stated that in a case of pulmonary sporotrichosis the fungus was found in smears from the pulmonary lesion in both spore and filamentous form. They certainly must have been in the tissue.

The eruptions of the disease are characterized by their polymorphism. They resemble, in the main, both tuberculosis and syphilis, and yet the impression obtained by close inspection is that they belong to neither group.

Gougerot's [20] classification is the one commonly used, and is as follows:

1. Localized lymphangitic sporotrichosis. In this type, the one to which the adjective American is added, there is usually a primary lesion, the so-called chancre, at the point of inoculation. Following this, in a variable time, subcutaneous gummas occur along the lymphatics draining the chancre. As a rule, the gummas do not remain intact; they either break down or are opened, with resultant polymorphous lesions.

2. Multiple subcutaneous gummatous sporotrichosis. The starting point of this type is a number of small, painless, firm, subcutaneous nodules. The nodules slowly enlarge and eventuate into the counterpart of the cold abscess by softening. They rarely ulcerate spontaneously.

3. Multiple ulcerating gummatous sporotrichosis. The lesions evolve in a way similar to those of type 2, but always ulcerate spontaneously and become tuberculoid, syphiloid or ecthymatous.

4. Sporotrichosis dermique. The keynote of this group is the presence of a variety of lesions simulating papulonecrotic tuberculids, scrofuloderma, verrucous tuberculosis, sarcoid, acne and ulcerative syphilids. Miliary abscesses are often found in some of the eruptions, and when noticed may be a valuable clue to the diagnosis.

5. Sporotrichosis epidermique. Lesions resembling kerion, vesicular eczema, intertrigo, erythematosquamous dermatitis and trichophytid make up the symptomatology of this variety.

6. Extracutaneous sporotrichosis. Hardly any part of the human body has escaped the ravages of this disease. The cases reported cover such infections of the eyelids, conjunctiva, lacrimal duct and sac, bulbar conjunctiva, cornea, iris and even the retina, the viscera, bones, synovial membranes and articulations, mucous membranes, muscles, mammary and other glandular structures, pharynx, larynx, trachea and testes. These infections may occur either with or without lesions of the skin, and are acute, subacute or chronic.

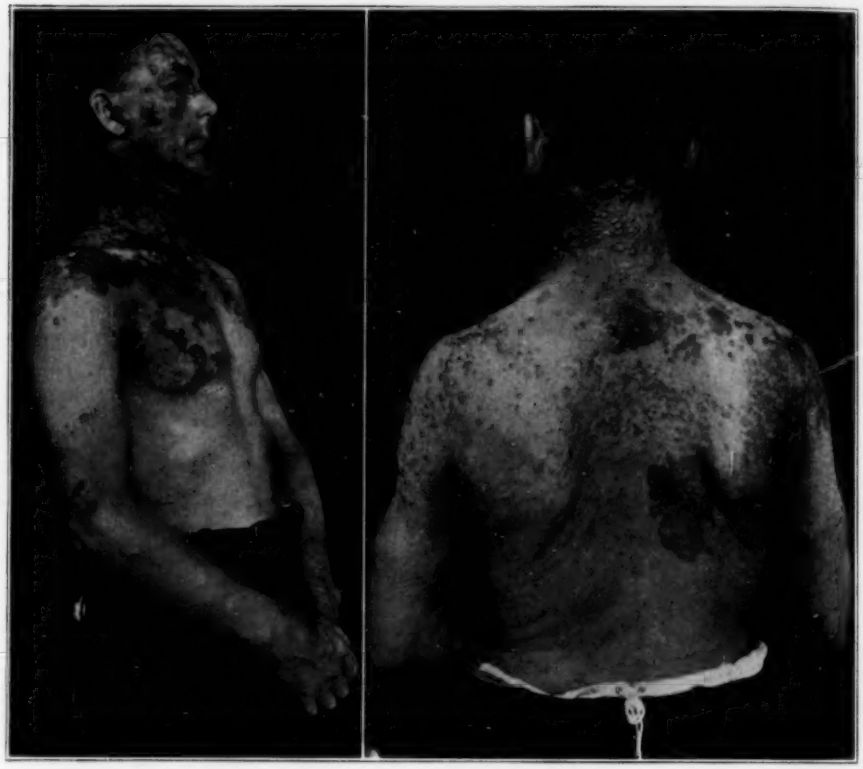
Formerly, sporotrichosis was mistaken for syphilis, tuberculosis or cancer, to the detriment of the sufferer, who went from pillar to post

18. Adamson: Proc. Roy. Soc. Med. (Sect. Dermat.) **4**:113, 1911.
19. Forbus, W. D.: Am. Rev. Tuberc. **16**:599, 1927.
20. Gougerot: La dermatologie en clientele, Paris, A. Maloine et fils, 1919.

seeking a cure for his malady. Many mutilating and useless operations were performed in the name of the healing art. Today, with the aids at hand in the laboratory and a better clinical acumen, the diagnosis should offer no hardships.

REPORT OF CASE

Mr. E. F., aged 53, a French Canadian by birth, had a family and past history of no significance. Previous to his present dermatologic condition, he



Appearance of patient, showing the extent of the involvement.

had never had any disease of the skin. The dermatosis, which was of two years' duration, began with an outbreak of lesions on the chest, back, arms, face and neck, and since that time there had been a continuous increase in the amount of eruption. Close questioning could not elicit the usual history of sporotrichosis, one lesion appearing first and then others. He insisted that many of them came out at the same time. Some would disappear either with or without breaking down and leave a mark, while others would crop out. There was no history of injury. The patient did not feel sick, nor did he have any febrile reaction. No departure from the normal was found in the cavity of the chest or in the abdomen. The Wassermann and Pirquet reactions were negative. The blood and urine were normal.

Examination disclosed a bizarre eruption made up of polymorphous lesions confined to the surface of the body above the waist-line, the lesions increasing in size and number from below upward. The lesions consisted of papules the size of a pea, tubercles varying in size from that of a pea to that of a hazelnut and tumors. Here and there some were broken down and discharged a small amount of viscid, purulent-like material. Irregular and somewhat pigmented scars were noted. No orderly arrangement of the lesions following lymphatic distribution could be seen. In color the outbreak was a mixture of red and brown, not unlike that shown by members of the group of chronic or infective granulomas. The various portions of the affected surface of the body presented the following lesions: the face, a number of tumors, some with small apertures; the back of the right ear, a similar tumor; the neck, an almost complete covering with papules and tubercles; the upper part of the chest and the right shoulder, plaques made up of papules and tubercles in varying stages of involution and evolution; the right mammary region, a serpiginous plaque with an active border and a healing centrum; the back, two infiltrated plaques surmounted by papules and tubercles, also numerous isolated papules and tubercles; the arms, papules and tubercles.

Inspection by means of a lens gave the impression of the presence of miliary abscesses in some of the lesions. One of these was opened, and cultures were made on mediums suitable for the growth of fungi. A papule was excised for microscopic study.

The report from the biopsy was to the effect that the lesion was a chronic granuloma with the changes essentially those already described, and, what was of still greater import, that delicate, branching septate filaments were present. The cultures gave a growth of a fungus identical in every respect with Sporotrichum.

The character of the individual lesions, the picture in toto, the results of culture and the microscopic observations warrant the placing of this case in the group of sporotrichosis dermique.

ABSTRACT OF DISCUSSION

Dr. Harry R. Foerster, Milwaukee: Dr. Mount has reported a case of a very unusual type of sporotrichosis, one that I believe has not been previously recorded in this country and one that is rare in Europe, sporotrichosis dermique. It is therefore important to determine the exact pathogenicity of the organism isolated in this case, since, as Dr. Mount stated in the text of his article, the sporotrichum may occur as a saprophyte. I have observed a case of ulcerating epithelioma in which a pure culture of Sporotrichum was obtained repeatedly and at long intervals, and in which it appeared that the organism existed in the ulcer as a saprophyte rather than as a pathogen. I therefore wish to inquire whether the organism was obtained on more than one occasion and from more than one lesion. I wish also to inquire regarding the nature of the treatment employed and the therapeutic effect, since the therapeutic test with potassium iodide may be considered of value in establishing the diagnosis of sporotrichosis. I believe that Dr. Mount's report is that of an unusual type of sporotrichosis; I do not know what other diagnosis would fit the case, and it is to be hoped that he will be able to investigate the case more fully to establish its identity more securely.

Dr. John E. Lane, New Haven, Conn.: This is certainly an unusual case. The disease is nearly symmetrical, of unusual, really extraordinary appearance, papular and tuberculous, of two years' duration; the patient was never sick, and there was no distribution through the lymphatics. There is no statement as to

whether any of the lymphatic glands were enlarged. There is no mention of a therapeutic test. The only evidence presented to establish the diagnosis of sporotrichosis is the statement that cultures were made and the organisms found in the microscopic preparation.

Sporotrichosis is an extraordinarily rare disease in this part of the country. In New York there are very few cases, and in Connecticut only two cases have been proved by culture. I think that before this paper is published we should have more evidence, photographs and descriptions of the organisms and of the culture, for we cannot be sure that we are dealing with sporotrichosis on such evidence as is now presented.

Dr. Fred D. Weidman, Philadelphia: I agree with Dr. Lane that the whole case stands or falls on the characteristics of the micro-organism, and that presentations which are remiss in this direction are responsible for much of the confusion that is existent in mycology in general. Probably the best way to avoid confusion of this sort is to submit cultures of all sorts to the American Type Culture Collection in Chicago. They are very glad to receive specimens of all organisms.

Specifically, I should like to know what color the organism was, whether later on it took on the black color of some Sporotricha, and whether attention was paid to the characters in hanging drop preparations, or at least microcultures.

Dr. Howard Fox, New York: This case has some unusual features, one of them being the simultaneous outbreak of numerous extensive lesions without any evidence of a primary focus. Whether the portal of entry was the skin or some mucous membrane it would be difficult to say.

Owing to the polymorphism of the case, a clinical diagnosis would be difficult. This was settled by histologic examination and culture. Other laboratory methods of diagnosis that might be used include smear preparations (stained by the Gram stain), animal inoculations, agglutination and complement-fixation tests and cutaneous reactions with sporotrichin (an emulsion of spores or a culture filtrate).

Dr. Louis B. Mount, Albany, N. Y.: I have a confession to make in connection with this case. It was presented to bring out just the discussion we have had. I intended doing the exact things that Dr. Fox has spoken of. Our cultures were left standing out, as the cultures of fungi are commonly left, and were gathered up at the pathologic laboratory one night and thrown out. This patient was a worker in a federal arsenal, and it was impossible to get in contact with him again, but I think that the type of lesions corresponds exactly with the description of the epidermic type. The facts that a fungus with fine filaments was found in sections of the lesions, that a culture was grown from a lesion that was opened under sterile precautions and smears made from the interior, and that colonies were produced on mediums suitable for the growth of fungi which, according to the director of the laboratory where the work was done, coincided, in his opinion, with Sporotrichum, also the study of the fungus in hanging drop preparations from the cultures warrant our placing this case in the sporotrichosis group.

News and Comment

NATIONAL LEPROSARIUM, CARVILLE, LA.

Dr. O. E. Denney, medical officer in charge, extends an invitation to the members of the section on dermatology and syphilology of the American Medical Association to visit the National Leprosarium at Carville, La., on Tuesday, May 10. The institution is about ninety miles from New Orleans, and it is planned to have buses leaving the Roosevelt Hotel at 9 a. m. About 360 cases at the institution will permit the demonstration of many types of leprosy in different stages of advancement. Lunch will be served at the hospital, and on the way back to New Orleans a stop will be made to permit a visit to one of the old plantation houses. Section members desiring to take advantage of this opportunity are asked to write either Dr. Ralph Hopkins, Pere Marquette Building, New Orleans, or the undersigned.

Dr. Francis E. Senear, *Secretary.*
55 East Washington Street, Chicago.

TEXAS DERMATOLOGICAL SOCIETY

The Texas Dermatological Society was organized and constitution and by-laws adopted at a meeting held in Galveston, Jan. 20, 1932. Dr. N. Riley Jackson, 110 West Seventh Street, Austin, was elected president and Dr. Everett R. Seale, 1215 Walker Avenue, Houston, secretary.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE NATURE AND ETIOLOGY OF CANCER. H. GIDEON WELLS, Am. J. Cancer (suppl.) **15**:1919 (July) 1931.

The experimental production of cancer in animals and observations of the manner of development of cancer in man support the old view that cancer is usually the result of protracted stimulation of tissue growth by nonspecific agents acting on tissues the susceptibility of which is determined by the hereditary background.

Occupational cancer from dyes, roentgen rays, tar and other cancerogenic agents rarely appears before from seven to fifteen years after the occupation has been begun, irrespective of the age of the afflicted person, and it appears in only a fraction of persons following a given hazardous occupation.

Young mice are as susceptible to the development of experimental tar cancer as older ones and in some lesions develop more readily than in others, but the majority require a period equivalent to one sixth of the normal space of a mouse's life, which corresponds to approximately twelve years of human life. Cancer is therefore not to be considered a disease of senescence of tissues, but a disease of long irritated tissues. Cancer is undoubtedly a universal disease in multicellular organisms, showing fundamentally the same characteristics in lower animals as in man and dependent for its development not so much on the amount or character of traumatism to which certain tissues are subjected as on the properties of the tissues themselves as determined by heredity.

The observation of identical tumors in identical twins supports the belief that the site and the type of tumor may be determined by heredity. On the basis of experimental work alone the author believes it reasonable to assume the existence of a hereditary influence on the susceptibility and resistance to cancer, with susceptibility to cancer behaving as a mendelian recessive.

Comparative pathology offers no support to the hypothesis that cancer depends on diet, or that it may be controlled by diet, and the experimental production of cancer in animals has repeatedly proved that cancer does not depend for its development on a specific parasite.

There are no available statistics on cancer that give even an approximately accurate indication of how frequently cancer is the cause of death, of how many people who die of other conditions have undiscovered cancer not responsible for death or of the relative frequency of attacks on different organs by cancer. Making due allowance for statistical error, it seems justifiable to the author to conclude that there is no real increase in cancer except to the extent that all diseases of advanced life are increasing because a larger proportion of the population reaches advanced life.

STUDIES ON THE HISTOGENESIS OF THE SO-CALLED "BASAL CELL CARCINOMA." SAMUEL R. HAYTHORN, Am. J. Cancer (suppl.) **15**:1969 (July) 1931.

The author studied 400 tumors from hair-bearing areas of the skin, and observed among them 144 typical examples of so-called "basal-cell" or "noncornifying" carcinomas conforming to the characteristics described by Krompecher as identifying such a lesion. Contiguity rather than continuity of basal cells with tumor cells was repeatedly demonstrated, and the point was emphasized that basal cells of epithelium are actually prickle cells and that differentiation in the epithelial tumors is away from prickle cells and toward spindle cells, with the formation of

fibrils like those found in hair follicles. A heavy basement membrane resembling the membrana vitrea of the hair was constantly present about the nests of tumor cells. The tumor stroma occasionally formed structures resembling hair papillae and tending to become cystic as do hair papillae in inflammatory areas. Evidences of imperfect hair shafts were found in a majority of the growths. The author is definitely of the opinion that the so-called basal cell carcinomas are actually carcinomas of the hair matrix associated with changes in the hair follicles and the less differentiated portions of the sebaceous glands. No relationships to sweat glands, congenital nevi or verrucae were observed.

METASTASIS OF A BASAL-CELL EPITHELIOMA. HENRY D. NILES, Am. J. Cancer (suppl.) **15**:2341 (July) 1931.

The author briefly reviews five cases of basal cell epithelioma with metastases to the lymph glands, and reports a sixth case in detail. The lesion in this case appeared as an indolent pea-sized warty growth on the side of the right ring finger of a 37 year old white man. During the course of several years a verrucous and ulcerated infiltration developed that was clinically diagnosed as tuberculosis verrucosa cutis. Biopsy proved it to be a basal cell epithelioma which Fraser believed to have originated in a hair shaft. After ineffectual roentgen therapy and miscellaneous medication over a period of two years, the involved finger was amputated, and a histologic diagnosis of basal cell epithelioma was again made. Three weeks following the amputation, a painless swelling appeared in the axilla and rapidly enlarged. This proved to be a lymph node which on removal five months later was diagnosed as a squamous cell carcinoma by MacNeal and metastatic basal cell epithelioma by Satenstein. Eight months after amputation the stump of the finger showed a recurrent ulceration, and six dime-sized sarcoid-like nodules appeared on the forearm of the involved side. Biopsy proved them to be basal cell epitheliomas. A year later recurrent swellings in the right axilla and neck that had not responded to deep roentgen therapy showed histologic features of atypical squamous cell epithelioma. Tissue examined following an intrascapular thoracic amputation showed true basal cell epithelioma in the cutaneous lesions and some of the glands and squamous cell epithelioma in other glands. A later recurrence in the supraclavicular fossa showed epidermoid carcinoma. At this time studies made by Ewing of tissue from different areas showed adenoid and plexiform basal cell carcinoma and plexiform squamous cell carcinoma. The patient died of metastatic lesions of the chest five and one-half years following the first recorded observation of his case. This case demonstrates a gradual transition from true basal cell epithelioma through intermediary and mixed forms to true squamous cell epithelioma over a period of years. It also demonstrates the metastasis of true basal cell epithelioma before transition had occurred.

[In this case the lesion and the areas of metastasis received repeated heavy doses of roentgen rays. Three of the other five patients with authentic metastatic basal cell epitheliomas are recorded as having repeatedly received radium or roentgen treatments, and most of the lesions received miscellaneous forms of irritant chemical and physical treatment. It is suggested that repeated irritation, particularly with roentgen rays or radium may have been the dominant factor in the transition from a relatively benign to an increasingly malignant type of epithelioma.]

THE OCCURRENCE OF MALIGNANCY IN RADIO-ACTIVE PERSONS. HARRISON S. MARTLAND, Am. J. Cancer **15**:2435 (Oct.) 1931.

The author reviews the cases of radiation osteitis and osteogenic sarcoma observed in former radium dial painters. The development of the sarcomas was attributed to chronic irritation caused by a radiation osteitis produced by internal bombardment from deposits of radio-active substances in the bones. He considers the alpha particle to have a more direct action in producing malignancy by speed-

ing up somatic cell division as a result of its destructive ionization. The record of four deaths from osteogenic sarcoma in seventeen deaths as a result of occupational poisoning with a radio-active substance and four additional sarcomas in thirty living radio-active former dial painters is contrasted with a statistical record of 0.07 per cent of primary osteogenic sarcoma, indicating that the radio-activity in these patients was undoubtedly the true cause of the sarcomas. It is suggested that possibly other forms of malignancy may depend on the presence in the human body of increased amounts of radio-activity too small to be detected by our present methods. He cites the high incidence of pulmonary cancer in workers in pitchblende mines. The author recommends government control and supervision of industries and occupations in which exposure to radio-active substances takes place because exposure to or the use of any radio-active substance that will increase the normal radio-activity of the body is undoubtedly dangerous. He also advocated some measure of control over the indiscriminate use of roentgen rays and radium.

AN INVESTIGATION OF THE PHYSICAL NATURE OF THE CANCER CELL. G. W. CRILE, M. TELKES and A. F. ROWLAND, Am. J. Cancer **15**:2659 (Oct.) 1931.

An investigation of the electric conductivity of tissues demonstrated that malignant tissue showed higher conductivity than normal tissue in the same organs and that this was especially high in the outer growing areas of cancer. Cancer tissue was found to possess more than double the electric capacity of similar normal tissue, while the electrical potential of cancer indicated an opposite sign of charge to that of the tissue in which the cancer was growing. Experiments have shown that it is possible to reduce the cancer potential to normal both by ionization and by radiation, and tumors have been reduced in size by ionization with various salts, particularly sodium chloride. The cancer cell is a cell of lower dynamic order than the normal cell, and its existence is possibly due to a partial degeneration of normal cells. Normal cells have but little growth energy, and therefore a relatively low order of growth energy in cancer cells is sufficient to compete successfully with normal adult tissues and organs that are unprepared for growth competition.

H. R. FOERSTER, Milwaukee.

ACTINOMYCOSIS IN CHILDHOOD. F. A. FIGI and R. A. CUTTS, Am. J. Dis. Child. **42**:279 (Aug.) 1931.

This article is a report of 14 cases of actinomycosis affecting children from 2 to 15 years of age. These patients comprised a little less than 3 per cent of approximately 450 patients with actinomycosis seen at the Mayo Clinic. Nine of the cases occurred in boys and 5 in girls. The cervicofacial area was involved in 10 cases (71 per cent), and the abdomen was involved in 4 cases.

One outstanding point of difference in the histories of children and adults was the absence of previous trauma in the latter group. Some of the children had repeated attacks of sore throat before the onset. Several children had carious teeth and diseased tonsils, which may have been etiologic factors. Two of the abdominal cases followed appendectomy. Sinuses were present in all of the abdominal cases and in 8 of the 10 patients with cervicofacial lesions.

Treatment consisted of the administration of a saturated solution of potassium iodide internally, beginning with 4 or 5 minims (0.25 to 0.30 cc.) three times daily and gradually increasing 1 drop daily to the point of tolerance. The drug was continued for two or three months after all symptoms had disappeared. Radium was administered with distance and screening over the affected area at intervals of from three to six weeks, as long as there was evidence of active infection. In a few instances in lieu of radium the patients received deep roentgen treatment with apparently equally beneficial results. In addition, hot moist compresses were used and free drainage established as soon as suppuration occurred. At the time of operation the abscess cavity was thoroughly swabbed with tincture of iodine and packed with iodoform gauze.

The prognosis in children with the cervicofacial type of infection is usually good, but in the abdominal and thoracic cases the outlook is poor. The 14 cases occurring in children are reported in detail.

LUPUS ERYTHEMATOSUS DISSEMINATUS ACUTUS IN A JUVENILE. C. C. STEWART and W. H. GOECKERMAN, Am. J. Dis. Child. **42**:864 (Oct.) 1931.

This is the report of a case of acute disseminated lupus erythematosus in a girl, aged 14, in whom the disease appeared on the face at the age of 5 years and gradually extended. The patient died two months after leaving the observation of the authors. The diagnosis of the attending physician at the time of death was acute miliary tuberculosis. Necropsy was not performed. The literature is reviewed, and the fact is brought out that only four undoubted cases of this disorder have been reported occurring in childhood.

ANDERSON, Los Angeles.

NICKEL SENSITIZATION FROM WHITE GOLD SPECTACLE FRAMES. A. W. MCALESTER, JR., and A. W. MCALESTER, 3rd., Am. J. Ophth. **14**:925 (Sept.) 1931.

The authors report three cases in which contact dermatitis of the eyelids, nose and ears was attributed to sensitization to nickel. In one case there was only pruritus; in another, erythema, and in the third, a papular and exudative dermatitis. A patch test in one case resulted in a positive reaction. All three cases cleared up when the spectacle frames were changed.

H. R. FOERSTER, Milwaukee.

PAGET'S DISEASE OF THE NIPPLE. G. LENTHAL CHEATLE and MAX CUTLER, Arch. Path. **12**:435 (Sept.) 1931.

The authors give a comprehensive review of the literature and present the results of their study of seventeen breasts affected by Paget's disease. They describe the clinical signs common to all their cases and also the pathologic changes as demonstrated by microscopic studies of serial sections of the whole breast in each case.

They establish the following diagnostic criteria: 1. "Paget's cells" are formed in the epithelial cells of the epidermis and in the openings of ducts. 2. Malignant-looking epithelial neoplasia occurs in the epidermis of these structures and in the cavities of the openings of ducts. 3. This epithelial neoplasia may be in direct continuity with epithelial neoplasia of malignant appearance in the upper reaches of the mammary ducts that terminate in the affected openings of ducts. 4. In the deeper parts of the breast there is either a highly suspicious epithelial neoplasia still confined within normal boundaries or carcinoma that may be clinically obvious.

They advocate radical mastectomy as the only rational treatment for the disease.

CARO, Chicago.

THE INFLUENCE OF DEHYDRATION ON THE PHENOMENA OF ANAPHYLAXIS IN GUINEA-PIGS. M. I. RUBIN and C. E. KELLETT, Bull. Johns Hopkins Hosp. **49**:170 (Sept.) 1931.

In a series of carefully controlled experiments the authors were able to show that dehydration protects a sensitized guinea-pig from anaphylactic shock. They believe that this protection is due to the diminished irritability of smooth muscle. They also point out that dehydration may explain the success of many of the other anti-anaphylactic procedures such as hypertonic salt solution.

Clinically, dehydration by means of diets that diminish the retention of water is being used for asthmatic children. While this work has only been carried on for a few months, the results are encouraging and will be reported in a future communication.

ANDERSON, Los Angeles.

THERAPEUTIC RESPONSE TO ERGOTAMINE TARTRATE IN PRURITUS OF HEPATIC AND RENAL ORIGIN. S. S. LICHTMAN, J. A. M. A. **97**:1463 (Nov. 14) 1931.

Ergotamine tartrate was administered orally in doses of 0.001 Gm. three times a day to relieve generalized pruritus of hepatic or renal origin. In four cases, two renal and two hepatic, the pruritus was relieved usually after the third dose. The drug was administered to one patient for six days, to the others, for three or four days. It acts by depressing the sympathetic nervous system, and in the four cases treated apparently the diminished sensitivity persisted indefinitely. The drug is best discontinued as soon as relief is obtained, as prolonged use is attended by dangers of ergotism. Apparently the drug is not hepatotoxic.

RATTNER, Chicago.

THE SKIN AS AN IMMUNOLOGICAL ORGAN. L. TUFT, J. Immunol. **21**:85, 1931.

During the course of some experiments in serum-sickness, it was observed that the skin seemed to possess an unusual capacity for sensitization to horse serum, this sensitization being accompanied by the production of anaphylactic antibodies, and these experiments suggesting the possibility that the skin may act as an important immunologic organ. Numerous clinical observations bear out the close relationship existing between the skin and processes of immunity in infectious and allergic diseases. These have been further substantiated by many experimental contributions reported in the past few years in the foreign literature, which appear to indicate not only that the skin may have the power to form antibodies, but that such antibodies may be specific and that the ability to form such antibodies resides specifically in the skin. My own experiments do not bear out the latter view, at least for antibacterial antibodies, for from a comparison of the antibody response after the intradermal, subcutaneous, intramuscular and intravenous injection of mixed typhoid vaccine, both in the human being and in the lower animals, it would appear that though it is possible that the skin participates actively in antibody production, it does not carry out this function exclusively in respect to other tissues or organs. The marked antibody response particularly after local injection can be best explained on the basis of a local tissue stimulation of the cells of the reticulo-endothelial system, these cells being particularly abundant in the skin. That the active antibody response after intradermal injection may be due in part to a slower absorption of the antigen is entirely possible, though this process may in turn allow for local fixation of a greater amount of antigen and thus greater local stimulation of antibody.

AUTHOR'S SUMMARY [ARCH. PATH.].

CERTAIN MONILIAS PARASITIC ON MAN. RHODA W. BENHAM, J. Infect. Dis. **49**:183 (Sept.) 1931.

This article deals with the identification of these organisms by morphologic and agglutination methods. The author describes a number of experiments from which she concludes that the parasite found in thrush, Monilia albicans, is a well defined species which can be recognized and differentiated from related forms by its morphologic and cultural characteristics. M. psilosis of Ashford is apparently identical with M. albicans isolated from thrush. She suggests that many of these yeastlike organisms found in erosio interdigitalis, chronic paronychias, perlèche, other dermatoses and certain types of superficial glossitis be placed for the present in this same species. Besides these organisms the author finds other species showing slight, but definite, morphologic differences on the skin and in sputum and feces. She tested thirty strains of monilias for virulence, nineteen of which, identified as M. albicans, from various sources, were pathogenic for rabbits. Eleven other strains, however, did not produce lesions in these animals. In making determinations of the reciprocal absorption of agglutinins the author found that seven strains of M. albicans had a similar antigenic content. The slight differences

detected could not be correlated with the sources from which these strains were obtained. Agglutinative reactions, when used in conjunction with other methods were found the most satisfactory means for the identification of these rudimentary forms.

THE INFLUENCE OF PUS AND BLOOD ON THE ACTION OF BACTERIOPHAGE. MARTHA APPLEBAUM and WARD J. MACNEAL, J. Infect. Dis. **49**:225 (Sept.) 1931.

The authors had under observation a girl who died as a result of a Staphylococcus aureus bacteremia which complicated multiple furuncles of the scalp. This fatal outcome occurred despite the fact that a therapeutic bacteriophage was used to which in vitro tests showed that the patient's staphylococcus was highly suscepible. This experience prompted the authors to make the reported study.

They found that a purulent exudate exerts a marked inhibitory influence on the lytic action of the antistaphylococcus bacteriophage, sufficient to explain the persistent survival of the bacteria in purulent collections within the body of a patient receiving treatment with potent bacteriophage. Even when diluted 1:1,000, a purulent exudate sometimes exerts a relative inhibitory effect in vitro. Heating the pus at 60 C. for thirty minutes diminishes this inhibitory effect only slightly. Similar dilutions of purulent exudate failed to show an analogous inhibitory influence on the lytic action of anticolon bacillus bacteriophage.

Undiluted citrated blood, undiluted defibrinated blood and diluted blood serum exercise an inhibitory influence on the antistaphylococcus bacteriophage, but there is considerable variation in the behavior of different bacterial strains and apparently in the behavior of different races of bacteriophage. Undiluted blood did not permit the multiplication of the colon bacillus under the experimental conditions employed, and the experiments with diluted serum failed to reveal a clearly evident inhibition of the anticolon bacillus bacteriophage.

CORNBLEET, Chicago.

CUTIS VERTICIS GYRATA. W. P. GRIEVE and E. BIDDLE, Proc. Roy. Soc. Med. **24**:1011 (June) 1931.

A man, aged 20, showed the rare congenital type of cutis verticis gyrata in marked degree. More than three fourths of the scalp was involved; the only normal portion was above and behind the right ear and abruptly defined from the "tumor." The skin of the left ear and the part of the face immediately in front of and above this ear showed scarring due to treatment in infancy. The epidermis showed normal cells, well developed rete pegs and a thin stratum corneum. There were numerous infoldings of the skin and many inclusion cysts. The appendages of the skin were well developed and numerous. Lying close under the epidermis were a few groups of pigmented nevoid cells. Lymphoid cells were scattered throughout the subcutaneous tissues, but were more numerous superficially. A few muscle fibers were found in the deeper tissues, and fat was comparatively scanty. The most striking appearance was found in the arrangement of the connective tissue, the hyperplasia of which was the cause of the increased thickness of the scalp. This connective tissue was very cellular and vascular, and was arranged in concentric bundles or whorls, which were especially well marked in the deeper layers of the corium. The vessels were numerous, dilated and thin-walled. The suggestive history, the nevoid cells and the arrangement of the connective tissue suggested that the condition was a congenital "tumor" of the lymphangioma type, somewhat allied to cystic hygroma. As a maldevelopment of the tissue rather than a tumor, it was extremely unlikely to recur or to become malignant.

GROUP OF THREE CASES: 1. ACNE CONGLOBATA; 2. ACNE CACHECTICORUM, 3. PERIFOLLICULITIS CAPITIS ABSCEDENS ET SUFFODIENS. A. M. H. GRAY, Proc. Roy. Soc. Med. **24**:1013 (June) 1931.

Examples of the three conditions were presented for differentiation.

Histologic examination of the lesions had been carried out by several observers, all of whom had found granulomatous lesions packed with round cells, plasma cells and leukocytes, with here and there giant cells of the foreign body type. There was a marked tendency toward hyperkeratosis, chiefly in follicles and also on the surface epithelium. The granulomatous tissue appeared to break down in places, with pus forming in the site. Cultures had shown mainly staphylococci, and in many cases only Staphylococcus albus. In my case, Staphylococcus aureus was grown on two of the smears, and, on one of them, also a nonhemolytic streptococcus. The other question of interest was that of relationship to tuberculosis. Because of its appearance, it had been thought that this was a tuberculous manifestation. Kreibich obtained an acid-fast bacillus from a lesion, but he did not consider it to be the tubercle bacillus. Ramel had claimed that by experiments with inoculation he produced tuberculosis from cases of severe acne, but Jadassohn failed to find evidence of the tubercle in the series of H. Hoffmann. Dressler described a case in which, apparently, definite tuberculids followed the eruption. My patient gave negative reactions to tuberculin; he had some slightly enlarged glands, probably due to his cutaneous condition, but roentgenograms of the chest showed little except a small increase in the shadows in the hilus. It was pointed out that these cases seem to differ from those of ordinary acne, first, in the type of the lesion, secondly, in the age factor, and lastly — a point that Michelson and Allen brought out in their paper — they produced identical lesions by inoculating the patient with his own pus. When they used pus from ordinary acne indurata they could not produce this type of lesion, and conversely they were unable to produce lesions of acne conglobata in a patient with acne vulgaris by using pus from the former case. Therefore, it seems that the condition was definite and specific, and its cause is still unknown. Large numbers of acid-fast bacilli were found.

W. H. GUY, Pittsburgh.

BOWEN'S DISEASE ON THE FACE. SÉZARY and LÉVY, Bull. Soc. franç. de dermat. et syph. **38**:1124 (July) 1931.

A patient, aged 49, presented a coin-sized erythematosquamous plaque on the left cheek of one year's duration. Clinically the diagnosis seemed to lie between discoid lupus erythematosus and pagetoid epithelioma of Darier, but microscopic study proved the condition to be Bowen's disease.

GANDY, Houston, Texas.

LOCALIZED ICHTHYOSIS. GOUGEROT, P. BLUM and J. BRUN, Bull. Soc. franç. de dermat. et syph. **38**:1128 (July) 1931.

A Hindu, aged 25, had been afflicted since the age of 2 years with a typical, symmetrical ichthyosis which was confined to the extensor aspects of the arms and forearms, the subumbilical part of the trunk and the lower extremities. The case is unique for three reasons: 1. It is an example of localized ichthyosis, a rare form of the disease. 2. The lesions are limited to the regions traumatized by friction of the clothing. 3. Along the borders of the ichthyotic plaques were lesions of keratosis pilaris, raising again the question of the relationship between these two conditions.

ANNULAR AND CIRCINATE FORM OF TINEA VERSICOLOR. GOUGEROT, DUCHÉ and GANOT, Bull. Soc. franç. de dermat. et syph. **38**:1131 (July) 1931.

A young adult showed disseminated macular lesions on the trunk from which Microsporon furfur was isolated. The interest of the case resides in the annular and circinate configurations of the lesions on the front of the thorax, with a tendency toward erythematosquamous forms.

ATROPHIC AND PIGMENTARY LICHEN PLANUS OF RETICULATED TYPE. GOUGEROT, R. COHEN and POULAIN, Bull. Soc. franç. de dermat. et syph. **38:** 1131 (July) 1931.

A case of widespread lichen planus of reticulated, atrophic type in a man, aged 69, is reported. The lesions occupied the nape of the neck, the chest and the back, a large part of the face and the forearms, and were accompanied by deep pigmentation. Oral lesions were also present. The patient had a partially positive Wassermann reaction. The cause of this unusual picture, particularly the pigmentation, furnished an interesting subject for speculation. Could the condition by syphilitic or tuberculous in origin, or due to endocrine or sympathetic disturbance? The answer, of course, was involved in obscurity.

OCCUPATIONAL ECZEMA DUE TO CEMENT. HEMOCLASTIC CRISIS FOLLOWING CONTACT TEST. GOUGEROT, R. COHEN and GANOT, Bull. Soc. franç. de dermat. et syph. **38:**1135 (July) 1931.

A patient who had worked with cement for some time with impunity suddenly developed a sensitivity to it, as expressed in a dermatitis that cleared up on removal from contact with the substance but recurred on resumption of his work. A patch test with the cement gave a positive reaction in a few hours, which was accompanied by a hemoclastic crisis, as manifested by a fall in blood pressure and a rising leukocytosis.

BENEFICIAL INFLUENCE OF FEVER ON PSORIASIS. GOUGEROT, Bull. Soc. franç. de dermat. et syph. **38:**1139 (July) 1931.

Two cases of psoriasis are reported in which the lesions disappeared following attacks of fever. In both patients the disease had been rebellious, failing to respond to all the stereotyped therapeutic measures. In one the fever was induced by intravenous administration of typhoid and Dmelcos vaccine, while in the other patient a septic temperature developed in the course of an anthrax infection complicated by perinephritic abscess. In the discussion, Ravaut stated that he had seen the same thing happen in eczema and seborrheic dermatitis.

CUTANEOUS TUBERCULOSIS OF THE FACE OF SYPHILOMA TYPE. LOUSTE, LÉVY-FRANCKEL and CAILLAU, Bull. Soc. franç. de dermat. et syph. **38:**1148 (July) 1931.

A patient presented a lesion of the face which clinically bore all the earmarks of a syphiloma. The Wassermann test of the blood was negative. A therapeutic test made no impression on the lesion. Biopsy showed a typical tuberculoid structure. The authors maintain that this case illustrates the fact that if there is such a condition as lupoid syphilid, there is also a syphiloma type of lupus.

PRIMARY SYPHILITIC ICTERUS. SYPHILITIC REINFECTION. MILIAN and DEGOS, Bull. Soc. franç. de dermat. et syph. **38:**1150 (July) 1931.

A typical penile chancre developed in a man, aged 30. The Wassermann test of the blood was positive. The infection was contracted extramaritally. No evidence of syphilis could be found in his wife. He received intensive treatment for six months, the Wassermann test of the blood becoming negative after three months; he then abandoned treatment. One month later he returned with another chancre on the prepuce. The dark-field examination gave positive results. The Wassermann test of the blood, at first negative, became positive with the outbreak of a secondary roseola. Several days after the appearance of this second chancre, a frank, generalized icterus, developed, accompanied by hepatomegaly, which rapidly regressed, while the liver remained enlarged. With the institution of treatment, the roseola disappeared and the liver began to shrink. Reexamination of the patient's wife revealed a chancre of the cervix, a secondary roseola and a strongly positive Wassermann reaction of the blood.

SYPHILOMA OF THE UPPER LIP IN A TABETIC PATIENT. MILIAN and GARNIER, Bull. Soc. franç. de dermat. et syph. **38**:1152 (July) 1931.

A syphiloma of the upper lip developed in a patient who had had tabes for many years, showing that cutaneous and nervous lesions are not always mutually exclusive.

PROGRESSIVE AND RECURRING DERMATOFIBROMA (FIBROSARCOMA) OF THE ABDOMINAL WALL. J. MARGAROT, P. PLAGNIOL and H. L. GUIBERT, Bull. Soc. franç. de dermat. et syph. **38**:1156 (July) 1931.

A woman, aged 43, presented a tumor of the abdominal wall which first appeared seventeen years prior to examination. Surgical intervention had been unsuccessful. This was the fourth recurrence. A detailed histologic study is reported, accompanied by several illustrations. The authors concluded that this tumor belongs in the classification of progressive and recurring dermatofibroma, or fibrosarcoma, described by Darier and Ferrand in 1924, and by Hoffmann in 1926, under the name dermatofibrosarcoma protuberans. In the discussion, Ravaut stated that he had obtained excellent results in three similar cases by heroic electrocoagulation.

PHOTOTHERAPY IN PSORIASIS: PATHOGENIC DEDUCTIONS. G. HUFSCHMITT, Bull. Soc. franç. de dermat. et syph. **38**:1164 (July) 1931.

Does not the fact that sunlight, ultraviolet rays and even x-rays commonly cause the spontaneous involution of psoriatic lesions at a distant point from the region irradiated, as reported by many writers, suggest the idea of some humoral disturbance in this disease? That patients with rickets are benefited by ultraviolet irradiation is a well established fact. It occurred to the author that an excess of phosphorus circulating in the blood of patients with psoriasis might provoke a resolution of the lesions. Although he found the blood calcium and phosphorus figures in several patients to be normal, he attempted to "saturate" the patients with these elements by administering them in divers ways. The results were negative.

A METHOD FOR DETERMINING ALLERGY BY INTRAGLANDULAR INJECTIONS. MILAN KITCHEVATZ, Bull. Soc. franç. de dermat. et syph. **38**:1166 (July) 1931.

The author undertook to ascertain whether, in the inguinal adenopathies, there is not an allergic state in the lymphatic tissues of the glands themselves as well as in the skin of such patients. The group here reported comprises twenty patients who had, or recently had had, chancroid. The antigen used was Dmelcos vaccine (streptobacillus of Ducrey). Two tenths of a cubic centimeter was injected directly into the gland, and the same amount was given intradermally. A positive reaction, noted in from twenty-four to forty-eight hours, consisted in enlargement of the gland plus sensitiveness to touch. As a control, a solution of sodium chloride was injected on the opposite side. Every patient gave a positive reaction, both intradermal and intraglandular, and all control reactions were negative. Some of the reactions remained positive for many days. Eight patients suffering from other diseases gave negative reactions to the test. These results, concludes the author, demonstrate the existence of an allergic state in the inguinal glands of patients with chancroid, which persists even after the infection has subsided, and which is analogous to the allergic state of the skin.

GLANDULAR ALLERGY IN THE INGUINAL ADENOPATHIES OF THE TYPE OF NICOLAS-FAVRE DISEASE. MILAN KITCHEVATZ, Bull. Soc. franç. de dermat. et syph. **38**:1172 (July) 1931.

Carrying the researches of his previous report still further, the author demonstrates, first, the existence of an allergic state in the regional glands of 10 patients with gonorrhea, all of whom gave a positive intraglandular reaction to an anti-

gonococcic vaccine, and second, in 11 patients with poradenitis (Nicolas-Favre disease) who showed the same phenomenon with Dmelcos vaccine. The latter fact is interesting in view of the fact that identical results were obtained in patients with chancroid, which would seem to speak for a specificity in that disease. It raises the question whether these two conditions may not differ only in morphology, the pathogenic agent being the same for both. Is it not reasonable to conceive that a Ducrey infection might sensitize the system by way of the lymphatic glands so as to favor a new infection which assumes the form of Nicolas-Favre disease? This consideration led the author to analyze the histories of 170 patients with poradenitis. He found that 32.9 per cent had had a prior infection with the bacillus of Ducrey, and 37 per cent had suffered from a previous venereal infection (gonorrhea or syphilis or both). Thus, in 70 per cent of this large group of patients with poradenitis it was possible to establish the fact that the regional lymphatic system had been attacked by one of the venereal diseases. Furthermore, when one considers the incidence of mixed infections (chancroid plus gonorrhea or syphilis), which often go unrecognized, the actual percentage is probably much higher.

There is, then, a new method for direct examination of the lymphatic system in question, namely, the intraglandular test, which demonstrates the presence of an allergic state in the regional glands, even in the absence of clinical adenopathy.

THE EXPERIMENTAL REPRODUCTION OF AN ADENOPATHY OF THE TYPE OF NICOLAS-FAVRE DISEASE. MILAN KITCHEVATZ, Bull. Soc. franç. de dermat. et syph. **38**:1176 (July) 1931.

Having shown the existence of an allergic state in the tissues of the regional glands, and that infection with the bacillus of Ducrey probably sensitizes the patient to the subsequent development of adenopathies of the type of Nicolas-Favre disease, as set forth in his two previous articles, the author next sought to reproduce the latter disease experimentally. The detailed report of this experimentation is the burden of this communication. This was done by selecting a patient with chancroid and injecting into his inguinal glands successive doses of Dmelcos vaccine in gradually increasing amounts. In the space of a month he saw develop an iliac and inguinal adenopathy which had all the clinical earmarks of Nicolas-Favre disease, the evolution of which was accompanied by constitutional symptoms typical of that disorder (malaise, fever, sweating, anorexia and loss of weight). The bacillus of Ducrey could never be isolated from the pus, and the scarification test was negative. On the other hand, an antigen prepared from the pus of a patient with a classic case of poradenitis gave a positive intradermal reaction in the experimental subject and, conversely, an antigen from the pus of the latter gave a positive intradermal reaction in the former.

THE REACTION OF SACHS-WITEBSKY IN THE DIAGNOSIS OF SYPHILIS. RENATO DE BLASIO, Bull. Soc. franç. de dermat. et syph. **38**:1181 (July) 1931.

The author presents a brief for the new flocculation test of Sachs and Witebsky, or the "citocholic reaction" (cito and cholesterol), so-called to distinguish it from the "lentocholic reaction" of Sachs and Georgi. The technic, which is quite simple, is described. From a comparative study of this test with the Wassermann and Hecht tests in 300 patients, the following conclusions are drawn: 1. This is a simple and rapid method which deserves widespread adoption in current practice. A positive reaction always means syphilis, while a negative reaction definitely excludes it. 2. Contrary to the Wassermann and Hecht tests, this test always gives a negative reaction in nonsyphilitic pregnant women. 3. It becomes more rapidly negative than do the Wassermann or Hecht reactions in the course of treatment.

DIAGNOSIS OF SYPHILIS IN THE CEREBROSPINAL FLUID BY THE CITOCHOL REACTION. RENATO DE BLASIO and A. MOREL, Bull. Soc. franç. de dermat. et syph. **38**:1186 (July) 1931.

From a comparative study of the Sachs-Witebsky reaction and the Wassermann reaction in 150 spinal fluids, the author concludes that although the former test is a rapid method it must be improved in order to attain the high degree of specificity that it possesses when applied to the blood serum.

LICHENOID DERMATOSIS OF THE FOREARMS. J. GATÉ, P.-J. MICHEL and C. E. BOYER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1015 (July) 1931.

A patient, aged 39, presented an eruption on both forearms of ten months' duration. It consisted of pinhead-sized, firm, rugose, lichenoid papules of perifollicular distribution, the individual lesions fusing to form plaques. Itching was absent. General examination and laboratory tests gave negative results. A biopsy remained to be done. The diseases considered in the differential diagnosis by the presenters were lichen scrofulosorum, perifollicular syphilid, pityriasis rubra pilaris, perifollicular seborrheic dermatitis, lichen nitidus and lichen spinulosus, but the condition seemed to fit satisfactorily into none of these categories. No help was obtained from the discussion. It was agreed that histologic section might solve the problem.

PSORIASIS TREATED WITH GOLD SALTS. J. NICOLAS, H. MOLLARD and F. LEBEUF, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1017 (July) 1931.

Believing that tuberculosis may play some rôle in the etiology of psoriasis, the authors treated twenty psoriatic patients with gold sodium thiosulphate. The number of injections, given intravenously in series, ranged from five to thirty-five. In seven cases the lesions disappeared completely; five patients were benefited but not cured, and eight showed no amelioration whatever, five of the latter manifesting intolerance (stomatitis, icterus, albuminuria and other conditions). Thus with this method one gets inconstant, though sometimes brilliant, results.

HYPERALGESIC HERPES ZOSTER PLUS GENERALIZATION OF ABERRANT VESICLES. J. NICOLAS, F. LEBEUF and AMIC, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1024 (July) 1931.

A patient, aged 30, was seized with violent radiating left-sided lumbar pain which prostrated him. Two or three days later a widespread confluent and gangrenous herpes zoster appeared on the lower right side of the thorax and abdomen. This was followed in two or three days by the development of aberrant vesiculopustular lesions disseminated over the entire surface of the body, the mucous membranes being exempt. A general medical examination gave essentially negative results. The old question of the association between zoster and varicella is raised again in this case. Almost immediate relief from the pain, followed rapidly by local and general amelioration, was obtained in this patient by autohemotherapy.

FOLLICULITIS DECALVANS, KERATOSIS PILARIS AND ONYCHOGRYPHOSIS. J. GATÉ, P. CUILLERET and C. E. BOYER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1033 (July) 1931.

A girl, aged 8 years, had a disease of the scalp of two years' duration. A large oval area of cicatricial alopecia covered the occipital and parietal regions. The edges of this zone were erythematous and were occupied by numerous points of suppurating folliculitis, the hairs being easily extracted. Microscopic examination

and culture of the hairs gave negative results for spores or mycelia. The eyebrows were gone, and the skin of the forehead and face showed erythema and marked dryness, with a fine desquamation. Characteristic lesions of keratosis pilaris occupied the nape of the neck and the extensors of the extremities. The finger-nails and toe-nails, especially the latter, exhibited a typical onychogryphosis. Several teeth showed dystrophic changes, the incisors particularly having suggestive, though not definite, hutchinsonian characteristics. In spite of negative serologic tests, and no other clearcut clinical evidence of congenital syphilis, the presenters wondered whether, in view of the abnormalities of nails and teeth, institution of antisyphilitic treatment might not be justified. The differential diagnosis between the scarring forms of alopecia was discussed, the decision being in favor of a diagnosis of folliculitis decalvans in this case.

Juxta-Articular Nodes. J. Rousset and B. Gonthier, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1036 (July) 1931.

What seems to be an authentic example of juxta-articular nodes in a syphilitic patient is reported.

Aphthous Stomatitis and Autohemotherapy. N. Ribollet, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1049 (July) 1931.

Three cases of severe, intractable aphthous stomatitis are recorded in which the condition was cleared up by means of autohemotherapy. Several discussers reported contrary results, but Ribollet insisted that this method is worthy of trial, particularly in advanced cases.

Multiple Cylindromas of the Scalp. Delaye, Hugonot and J. Lacassagne, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1191 (July) 1931.

A man, aged 42, had a curious disease of the scalp which began at the age of 16 in the form of a small tumor. This was succeeded by the gradual appearance of other tumors. Recurrence followed surgical excision. At the time of examination, about 250 growths were disseminated over the scalp. They were rosy, rounded, flabby, sessile tumors, varying from the size of a lentil to that of a prune. The histologic picture showed an epithelioma-like structure similar to that of the cylindroma described by Dubreuilh and Auche in 1902. In the discussion there was a variance of opinion with respect to which of the following methods of treatment was most suitable: roentgen therapy, surgical intervention or electrocoagulation.

Buccal Lichen Planus and Lichen Corneus in Early Syphilis. J. Gaté, P. J. Michel and C. E. Boyer, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1199 (July) 1931.

In a young man who had early syphilis and had received a series of injections of arsphenamine, buccal lichen planus and lichen corneus hypertrophicus of the right forearm developed. It was curious that these conditions appeared in the face of arsenical therapy, which is frequently employed against them. Both disorders responded to irradiation of the cervical spine.

Lupoid Syphilis. J. Gaté, P.-J. Michel and C. E. Boyer, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1203 (July) 1931.

A girl, aged 9 years, had a lesion on the right thigh of several years' duration. It consisted of a violaceous plaque, ulcerating at two points, and showing nodules under the diascope. Inguinal adenopathy was present. A clinical diagnosis of

lupus seemed plausible. However, the child had certain stigmas of congenital syphilis and a slightly positive Wassermann reaction of the blood, and the lesion melted away under antisyphilic treatment. Thus one was justified in changing the diagnosis in this case to lupoid syphilis.

SPLENIC EXTRACT IN PRURIGINOUS DERMATOSES. J. GATÉ and J. CHARPY, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1222 (July) 1931.

A splenectomized animal develops eosinophilia which can be controlled by injections of splenic extract. This fact inspired certain German authors to use splenic extract in the treatment for pruriginous dermatoses accompanied by eosinophilia. Good results have been alleged. Gaté and Charpy tried this method in thirty-two patients suffering from certain rebellious, itching dermatoses, such as chronic eczema, lichen planus, dermatitis herpetiformis, etc. Results on the whole were good, bad and indifferent. They concluded that this method, while not a panacea, is nevertheless deserving of recognition as a valuable addition to our therapeutic procedures in these stubborn disorders, particularly for relief of itching.

RECURRING HERPES AND CONGENITAL SYPHILIS. J. WATRIN, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1075 (July) 1931.

Two children with congenital syphilis also had recurring herpes simplex of the face, the latter disease being cured by antisyphilitic treatment. Watrin believes that this was due to the "shock" of the arsenical injections, after the manner of nonspecific protein therapy.

COEXISTENT PSORIASIS AND HYPERTHYROIDISM TREATED WITH THYMUS EXTRACT. P. MICHON, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1085 (July) 1931.

A man, aged 38, in whom hyperthyroidism and psoriasis coexisted, was given thymus extract in subcutaneous injections, and both diseases responded promptly to this therapy.

COEXISTENT VITILIGO AND PERINEAL PRURITUS WITH LICHENIFICATION. DISAPPEARANCE OF THE VITILIGO AFTER ELECTRODESICCATION. J. L. CRÉHANGE and L. MATHIEU, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1086 (July) 1931.

A woman, aged 37, complained of perineal pruritus of three months' duration. On examination a typical vitiligo patch was observed, occupying the perineal region and the inner aspects of both thighs, which she stated had been present for seven years. Large lichenified plaques were also present in the same region, electing particularly the hypochromic zones of the vitiligo. The pruriginous and lichenified areas were treated by means of electrodesiccation at weekly five minute seances. The pruritic symptoms rapidly abated, and at the sixth sitting the authors noted to their surprise that the vitiligo was much less pronounced. At the tenth treatment it completely disappeared.

WASSERMANN-FAST SYPHILIS AND ACID-BASE EQUILIBRIUM. L. SPILLMANN, VERAIN and SEGALL, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1087 (July) 1931.

From an experience with two patients, the authors conclude that there is a disturbance in the acid-base equilibrium in Wassermann-fast cases of syphilis, which appears to be due to some humoral abnormality produced by syphilis, the nature of which is obscure. A restoration of the p_H to normal by appropriate medication results in reducing the serologic reactions to negative.

POLYMORPHOUS IODIDE ERUPTION. SPILLMANN, WEISS and DURAND, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1092 (July) 1931.

In a man, aged 51, a widespread eruption developed which began three days after the patient took a cough syrup containing potassium iodide. The lesions occupied the face, neck, trunk and extremities, and were polymorphous, consisting of pustules, crusted ulcers and even vegetating and papillomatous elements. There were no constitutional symptoms. The condition was regarded, not as an intoxication, but as a specific cutaneous sensitivity.

ACID-BASE EQUILIBRIUM AND ECZEMA. L. SPILLMANN, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1097 (July) 1931.

A patient with a stubborn case of eczema was made distinctly worse by taking sodium hyposulphite orally, but administration of alkali cleared up the acute outbreaks promptly. The author believes that while the mechanism of eczema is much more complex, a disturbance in acid-base equilibrium surely is a factor in some cases.

LIPOSOLUBLE BISMUTH IN SYPHILOTHERAPY. SPILLMANN and FIDEL, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1098 (July) 1931.

Spillmann and Fidel contend that the liposoluble preparations of bismuth are far superior to the insoluble forms in suspension in therapeutic results. A number of cases are cited, representing various phases of syphilis, which showed prompt reversal of the Wassermann reaction of the blood from positive to negative.

KELOIDS OF THE NECK FOLLOWING ELECTROLYTIC EPILATION. J. MARGAROT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**: 903 (July) 1931.

In a young woman keloids developed under the chin and on the anterior part of the neck following treatment for hypertrichosis in that region by means of electrolysis. The patient had hyperthyroidism. Her father was subject to keloids also, which responded to roentgen treatment. In this case, carbon dioxide snow, associated with injections of fibrolysin, had given the best results.

STATISTICAL STUDY OF KELOIDS. NAEGALI, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:905 (July) 1931.

This paper is a statistical study of the frequency of keloids. In an examination of 3,335 healthy school children, the author found keloids in 151, an incidence of 4.5 per cent. Below 10 years of age the condition predominated in boys, while in children from 10 to 15 years the difference between the sexes was slight. The preponderance of these keloids existed in vaccination scars. The incidence was much higher in the later age group than in the earlier. Among 834 adults examined, 112, or 13.3 per cent, had keloids. In the aged they were rare. An entire hospital population of 530 patients suffering from various acute and chronic diseases, both children and adults, were also examined, and the incidence of keloids was found to be much higher than in the group of healthy persons. Among 49 patients with tuberculosis, 11 (22.4 per cent) had keloids.

TATOOS AND KELOIDS. J. LACASSAGNE and J. ROUSSET, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:919 (July) 1931.

That keloids have a tendency to develop in tattoo marks, a widely accepted view, is disputed by the authors, who investigated the matter in a large number of persons. A case is cited in which the patient showed an unusual keloidal tendency, as manifested by the presence of numerous keloids in acne scars, yet tattoo marks in the same patient were entirely free from keloids.

POSTIMPETIGINOUS PSEUDOKELOIDAL SCARS. G. MILIAN, Bull. Soc. franç. de dermat. et syph (Réunion dermat. et Strasbourg) **38**:920 (July) 1931.

In a man, aged 27, a bullous impetigo of the hands was followed by the appearance of lesions that had all the clinical earmarks of keloids, but to the surprise of the author, histologic examination revealed merely a localized hyperkeratosis of the eroded regions, with no semblance of keloid structure.

POSTFURUNCULAR AND TRAUMATIC KELOID WITHOUT KELOID IN OPERATIVE SCAR. PIGNOT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:923 (July) 1931.

In a woman keloids developed in scars resulting, respectively, from a traumatic injury and from a furuncle, yet the scar of a laparotomy wound was not affected.

POSTACNEIC THORACIC KELOID. L. HUDELO and R. RABUT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:928 (July) 1931.

The fact that keloids are so prone to elect the regions in which acne occurs and indeed often appear as sequelae of acne or even associated with it, as in acne keloid, would seem to indicate a peculiar relationship between these two conditions. The authors think that keloids are due to a local plus a general cause, though they are unable to say what these causes are.

SPONTANEOUS KELOID. W. DUBREUILH, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:930 (July) 1931.

A spontaneous keloid developed on the chest of a woman, aged 20. There was no antecedent pathologic or traumatic lesion.

POSTACNEIC THORACIC KELOID RECURRING AFTER EXCISION. NO KELOID IN OPERATIVE SCAR AFTER APPENDECTOMY. H. MONTLAUR and P. BAGOT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:931 (July) 1931.

A keloid developing in an acne lesion on the chest was excised after five years and promptly recurred, yet surgical intervention in the abdomen ten years later resulted in a normal laparotomy scar. This is probably explained either on the basis of a difference in site or by the fact that there had been a modification of the terrain in the intervening years.

PATHOLOGIC ANATOMY OF KELOIDS. L.-M. PAUTRIER and F. WORINGER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:932 (July) 1931.

This article is a detailed discussion of the pathologic anatomy of keloids. The authors state that no study of the morphology of a keloid, however particular, can throw any light on the p.oblem of pathogenesis. One question, however, poses itself: Should the keloid be classed among hyperplastic tumors or among benign neoplastic tumors? The latter group includes growths that proliferate without the intervention of any apparent irritative process, while in the former group the reverse is true. From the point of view of pure histology, the keloid might properly be called a benign neoplastic tumor, but the well known clinical fact of its appearance posttraumatically places it, the authors think, in the category of hyperplastic tumors. No one can explain the two factors that influence the formation of keloids, namely, local irritation and general predisposition.

THE CAUSES OF KELOIDS. LORTAT-JACOB, FERNET and SOLENTE, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:943 (July) 1931.

This article is a speculation on the possible nature of the relation of keloids to tuberculosis, infectious processes per se, trophoneurosis, endocrine disturbance, etc., without any positive conclusions. The mechanism of keloid formation, according to the authors, is as follows: There is a local giving way of the antagonistic action that the epidermis normally exerts against proliferation of the derma. Once this tendency appears, it is strengthened by the stimulation of even minimal trauma, and a keloid gradually takes form.

BIOLOGIC EXAMINATION WITH EXTRACTS OF KELOIDAL SUBSTANCE. NAEGELI, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:947 (July) 1931.

Intradermal tests with extracts from keloidal tissues in 200 patients suffering from various diseases, many of whom had keloids, gave totally negative results, allowing no conclusion to be drawn regarding the presence of an antigen.

IMPLANTATION OF KELOIDAL TISSUE IN THE GUINEA-PIG. J. WATRIN and P. DROUET, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:948 (July) 1931.

Intrigued by the idea that there might be some relationship between keloids and tuberculosis, these authors implanted in the abdominal wall of guinea-pigs fragments of keloidal tissue, choosing the guinea-pig because of its known susceptibility to tuberculosis. Subsequent autopsy examination revealed no evidence of tuberculous infection in the animals.

EXPERIMENTAL RESEARCHES WITH ANIMALS. NAEGELI, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:949 (July) 1931.

In a dozen persons who showed tuberculous infection in some form, and also had keloids, tissue extracts were prepared from the latter and injected into guinea-pigs and rabbits. When examined several weeks later at autopsy, none of the animals showed any pathologic alterations. From this Naegeli concludes that keloid tissue probably does not harbor the tubercle bacillus, either the human or the bovine type.

NEGATIVE RESULTS FROM INOCULATION OF THE GUINEA-PIG AND RABBIT WITH KELOID AND ACNE KELOID TISSUE. L.-M. PAUTRIER and R. GLASSER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:950 (July) 1931.

A number of dermatologists believe that keloids are due to a micro-organism, and efforts have often been made to incriminate the tubercle bacillus. Hyde even claimed to have reproduced tuberculosis in the guinea-pig by inoculation with keloid tissue and to have recognized the bacillus of Koch in the lesions. Pautrier doubts the accuracy of this work and records here another experiment tending to refute it. Ground-up tissue from two cases of keloid and one case of acne keloid was injected subcutaneously on the abdomen and intradermally on the back into guinea-pigs and rabbits. No local or general reaction of any sort could be discovered, although the animals were observed for months.

CALCIUM CONTENT OF KELOIDAL TISSUE. L.-M. PAUTRIER and ZORN, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:953 (July) 1931.

The calcium content (70 per cent) of the keloidal tissues examined was found to be higher than the figure for normal skin. This proves nothing, of course, but raises a question as to the significance of hypercalcemia in the production of keloids.

GANDY, Houston, Texas.

DIPHTHERIA OF THE SKIN. H. STUX, Nourrisson **19**:228 (July) 1931.

A review of the literature shows that cutaneous diphtheria occurs most frequently in infants aged 2 years and under. In the nursery at Odessa, where normal infants up to the age of 1 year are admitted, sixteen cases of primary diphtheria of the skin were encountered in five years; eight others in which the skin infection was secondary to other diphtheria infection were also seen. Most of the cases occurred during the winter months. Infantile eczema seemed to be a predisposing cause. The course of the disease is usually benign. The cases responded promptly to treatment with antitoxin. In institutions prophylactic measures are important.

McCLELLAND, Cleveland [AM. J. DIS. CHILD.].

ERYTHEMA NODOSUM: II. HEART MURMURS IN ERYTHEMA NODOSUM; THE RELATION OF ERYTHEMA NODOSUM TO ACUTE RHEUMATIC FEVER. P. FORRARA, Riv. di clin. pediat. **29**:89 (Feb.) 1931.

The author has assembled statistics from the literature on the incidence of acute arthritis in erythema nodosum, of erythema nodosum in acute rheumatic fever, of tuberculosis (also phlyctenular keratitis) in erythema nodosum, of tonsillitis in erythema nodosum, and of heart murmurs following erythema nodosum. Of the eighteen cases of erythema nodosum personally observed by the author, seven were initiated by tonsillitis (erythematous in six and follicular in one). In three, marked arthritic pain was present. In one, albuminuria was present. In four, cardiac murmurs appeared in the course of the erythema nodosum and persisted. The murmurs were systolic in time, were heard over the body of the heart and not transmitted, and were musical. The author thinks that the murmurs represent a true but slight cardiac lesion. He concludes that erythema nodosum has only a slight resemblance to acute rheumatic fever. While not of a tuberculous nature it is a disease that has a definite association with tuberculosis.

HIGGINS, Boston [AM. J. DIS. CHILD.].

TWO CASES OF MALIGNANT LYMPHOGRANULOMATOSIS WITH SEROFIBRINOUS PLEURISY. L. MORQUIO, Arch. argent. de pediat. **1**:573 (Dec.) 1930.

The author presents a detailed discussion of the history, pathology, clinical picture and treatment of malignant lymphogranulomatosis or Hodgkin's disease. He describes two cases occurring in a girl and a boy, 13 and 11 years of age, respectively, who presented a typical clinical and pathologic picture of the disease, or what the author calls an adenosplenopleuritic syndrome. Both patients presented, in addition, an extensive serofibrinous pleural effusion. Symptoms of pressure on the mediastinal structures or dyspnea were entirely absent in one of the patients in spite of the fact that the pleural effusion was extensive enough to produce a total displacement of the heart to the right.

The author brings out the fact that the pleural effusion of Hodgkin's disease closely resembles that of tuberculosis in that it is also very extensive and recurs rapidly after paracentesis. In fact, it has been called "pseudotuberculous" by some authors. The tuberculin reaction and the results of guinea-pig inoculation are consistently negative in this form of pleurisy. This effusion fluid is rich in fibrin

and leukocytes; among the latter either the polymorphonuclear or the mononuclear forms may predominate, so that it is an exudate rather than a transudate. The effusion is due to the pleural irritation set up by the lymphogranulomatous infiltrations.

A marked melanoderma, i. e., a pigmentation similar to that present in Addison's disease, was a prominent feature in one of the patients. This, according to the author, could be accounted for by the presence of extensive granulomatous infiltration in the suprarenal glands, which was revealed at autopsy.

SCHLUTZ, Chicago [AM. J. DIS. CHILD.].

A BULLOUS ERUPTION OF THE HANDS AND PENIS PROBABLY DUE TO STRANGLES (ADENITIS EQUORUM). W. LEIPOLD, Dermat. Wchnschr. **93**:1533 (Oct. 3) 1931.

Strangles is common in horses and is due to Streptococcus equi. There has been no report of its transmission to man. A 25 year old man had assisted in treating horses affected with this disease, in the course of which he had soiled his left hand with pus from an infected gland. The same evening he noted pruritic areas on this hand which became bullous in the morning. Two days later a bulla appeared on the glans penis, and several new lesions appeared on both hands. The lesions all cleared up in a short time under dressings with an ointment of 10 per cent sulphonated bitumen, N. F.: A streptococcus was recovered in pure culture which coincided with Streptococcus equi in its appearance and cultural characteristics.

INFECTION WITH SYPHILIS IN SPITE OF A PROPHYLACTIC COURSE OF BISMUTH. BRUNHILDE HOFMANN, Dermat. Wchnschr. **93**:1543 (Oct. 3) 1931.

A typical chancre developed in a prostitute immediately after the administration of a course of eight injections of an oil-soluble bismuth preparation. It is assumed that the infection was received just before the course of treatment was started, though it is theoretically possible that the bismuth delayed the appearance of the primary lesion.

ZONIFORM DISTRIBUTION OF A MULTIPLE METASTATIC CARCINOMA OF THE SKIN. O. KIESS, Dermat. Wchnschr. **93**:1577 (Oct. 10) 1931.

A case is reported in which metastatic carcinoma nodules developed in the skin of one buttock in a zosteriform arrangement. The primary growth was probably either in the liver or the kidney.

REGULATION AND DISTURBANCES OF THE PERIPHERAL CIRCULATION. J. TANNENBERG, Dermat. Wchnschr. **93**:1581 (Oct. 10) 1931.

The author reviews the literature in regard to the physiology of the peripheral circulation and cites a number of his own experiments. He points out that the rate of flow in the capillaries is independent of the arterioles and venules. Circulatory disturbances may be due to substances which act (1) on the tissue and the walls of the blood vessels, (2) on the blood plasma and the blood elements and (3) on the nerve elements that have to do with the circulation.

PITYRIASIS ROSEA. S. A. GLAUBERSOHN, Dermat. Wchnschr. **93**:1589 (Oct. 10) 1931.

The author found that pityriasis rosea made up 0.79 per cent of the total number of cases seen in the Kiev clinic. The disease occurred more frequently in women than in men and most often between the twenty-fifth and thirtieth years. The disease appeared in all seasons, but the incidence reached its minimum in the fall. The author believes the condition to be an endogenous infection of low virulence, though he presents no direct evidence for this conclusion.

THE TREATMENT OF ROSACEA. ELISABET BREUER, Dermat. Wchnschr. **93**:1592 (Oct. 10) 1931.

The local treatment consists of a short course of mild carbon dioxide snow applications followed by a series of from thirty to forty treatments by catephoresis with caffeine sodium salicylate solution and then epinephrine hydrochloride solution. General treatment is also stressed.

THE ACTION OF SEXUAL HORMONES IN A CASE OF PSORIASIS ARTHROPATHICA. P. KELLER, Dermat. Wchnschr. **93**:1693 (Oct. 31) 1931.

A woman, 30 years of age, had a thyroidectomy following which the menses became irregular, stopping entirely a year following the operation. Psoriasis developed for the first time six months after thyroidectomy, associated with severe arthritis. Ovarian extract treatment improved the symptoms, though the psoriasis of the skin did not entirely disappear. The author discusses the possible action of the hormones concerned.

A CASE OF MYELOGENOUS LEUKEMIA WITH INVOLVEMENT OF THE SKIN. LUDWIG NÉKÁMJUN, Dermat. Ztschr. **62**:158 (Oct.) 1931.

Involvement of the skin in myelogenous leukemia is extremely rare. A patient was observed with acute myelogenous leukemia which terminated in two weeks. She presented numerous blue-red, bean-sized tumors which histologically consisted for the most part of myeloblasts with a negative oxidase reaction. The appearance suggested an infiltration rather than a local new growth.

SEROLOGIC TESTS ON SYPHILITIC AND HEALTHY MICE WITH THE MEINICKE MICROREACTION. SARTONI KERTOPATI, Dermat. Ztschr. **62**:174 (Oct.) 1931.

Thirty normal mice gave negative reactions to the Meinicke test. Of ninety-three mice in which syphilitic material from various sources was injected, only four showed positive reactions. These four continued to show positive results on repeated tests.

TAUSSIG, San Francisco.

TREATMENT FOR INFANTILE ECZEMA WITH GRENZ RAYS. L. DOXIADES, Ztschr. f. Kinderh. **51**:175 (June) 1931.

Doxiades assumes that the favorable therapeutic action of Grenz rays in chronic recurring eczema in childhood is to be explained on the ground that the excessive production of histamine-like substance in the skin and, consequently, the cause of the skin irritation are prevented. A better result would be obtained if, along with this treatment, a diet poor in protein could be given.

PECULIAR GENERALIZED FLUCTUATING GLANDULAR SWELLINGS IN A BOY ELEVEN YEARS OLD. O. WIESE, Ztschr. f. Kinderh. **51**:432, 1931.

A boy, aged 11 years, had had scrofula and tuberculosis of the bone as a small child, but no trace was left. During the past year enlarged glands, up to the size of a small apple, had appeared over the body, symmetrically in the axillae and groins, singly and in groups, but not coalescing. The larger ones were fluctuant. Roentgen examination of the lungs gave negative results; the tuberculin test was negative nine times, and tests of the blood were negative. A milky fluid was obtained by puncture; this was not a pure chyle, but porridge-like and chalky, showing under the microscope detritus, some lymphocytes, fat droplets and no bacteria. Three tests done on guinea-pigs were negative. Histologically, an excised gland was made up of extensive caseous foci embedded in fibrous connective tissue poor in nuclei. There was no evidence of a specific inflammation. An animal test gave negative results. The diagnosis seemed to lie between tuberculosis and lymphogranuloma. In the next seven months the boy gained 4 Kg., and no new swellings appeared; he was then lost from observation.

EMERSON, Boston [AM. J. DIS. CHILD.].

PRECANCEROUS CHANGES CAUSED BY THE X-RAYS. O. SCHÜRCH, Ztschr. f. Krebsforsch. **33**:1, 1930.

Schürch reports the results of studies of the cancerigenic action of the roentgen rays on the rabbit's ear. A long period, two years or more, and a prolonged and heavy dosage, short of single applications sufficiently dense to cause immediate necrosis, were necessary, but even with these precautions, development of cancer was only occasional. Such animals as did not become cancerous showed changes of somewhat varied types; in some, there appeared small, warty lesions, with perforation supervening later, with or without preceding atrophic changes; in others, the latter was the outstanding feature. When the warty growths were present, they continued to develop throughout the period of exposure, but did not become cancerous. In still other cases, there was early and extensive, but delimited, necrosis. In the lesions that later developed into cancer, the outstanding peculiarity, after atrophy and perforation, was the appearance of successive and recurring small erosions, at the sites of which usually, but not invariably, local hyperplasia and development of cancerous growth occurred. Cancer evidently did not occur as a regular stage of the inflammatory reaction, but only through a peculiar evolution of this, so that roentgen dermatitis is definitely precancerous only in the clinical sense; in it cancer is a secondary, nonessential change, and the morphologic changes of roentgen precancer in the rabbit are those of the secondary erosive lesions.

PRECANCEROUS CHANGES. O. SCHÜRCH, Ztschr. f. Krebsforsch. **33**:35, 1930.

In a general discussion of the nature of precancerous change, to which the author appends an exceptionally complete bibliography, he takes the well grounded position that precancer does not so much represent a definite disease type as an intermediate stage between normal and cancerous tissue. Morphologically, this stage is represented by proliferative epithelial changes, atypically arranged and with abnormally formed cells and nuclei, accompanied by changes in the underlying connective tissue. But even these changes are not necessarily precancerous, as they are distinctly reversible. Just as important as the morphologic changes are the clinical features—the character of the irritation, the nature of the tissue, the heredity and the possible metabolic or endocrine dysfunction. Clinically, a sharp differentiation should be made between lesions that are actually cancerous, as basal cell carcinoma or Paget's disease of the nipple, lesions that experience has shown are precancerous with some regularity, as senile hyperkeratosis, papillary leukoplakia and lentigo maligna, and lesions that become cancerous only occasionally and exceptionally, as lupus vulgaris.

EGGERS [ARCH. PATH.].

SYPHILIS AND TUBERCULOSIS. ZAHRADNICKY, Časop. lék. česk. **68**:1096 (Aug. 2); 1129 (Aug. 9); 1159 (Aug. 16); 1188 (Aug. 23) 1929.

Direct inoculation with tuberculosis practically never occurs in the chancre stage, but may take place during the secondary or tertiary stage. Indirect tuberculous infection may take place after a decrease in resistance following syphilitic infection or in congenital syphilis. Syphilitic children have a predisposition to rickets and localized tuberculosis. Sargent stated that syphilization is the terrain of choice for tuberculosis; syphilization in the parents predisposes to tuberculosis in the offspring, and the family history reveals syphilis in children with scrofulotuberculosis. Syphilotuberculosis is divided into scrofula engrafted on old or recent syphilis, or syphilis engrafted on a preexisting scrofulotuberculosis. The differential diagnosis of tuberculosis and syphilis is taken up in minute detail. The preference of tuberculosis for pulmonary tissue and that of syphilis for nervous tissue is discussed. The differential diagnosis of lesions of the bones, joints, glands, skin and mucous membranes is given in detail. A bibliography is appended.

STULIK, Chicago [AM. J. DIS. CHILD.].

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

J. P. Guequierre, M.D., *Secretary*

Oct. 2, 1931

Jacob M. Schildkraut, M.D., *Presiding*

Case of Vincent's Infection of the Umbilicus, Associated with Pemphigus. Presented by Dr. R. L. Gilman.

M. S., a Negress, aged 31, was admitted to Dr. William's service in the gynecological wards of the Philadelphia General Hospital late in August, 1931. She had had a sore mouth for eight months prior to admission, and two months previously she had experienced a cutaneous eruption. The lesions on the body appeared as crusted patches about the scalp, axillae, elbows, umbilicus and pubis. More recently there had been some extension to the back, likewise some involution of the older lesions. At the time of presentation the picture included a group of the older crusted lesions (almost vegetative), abrasions, fissures and new bullous lesions The mouth was much improved. The patient's general condition was poor.

The past medical history included syphilitic infections in both the patient and her husband. The Wassermann reaction was 2+ in the cholesterolized antigen, the Kahn reaction 3+. Smears from the mouth were negative. Smears from the umbilicus were positive for Vincent's disease. Earlier in the course of the infection a diagnosis of syphilis with a predilection for the seborrheic areas was considered. The later consideration was amended to the diagnosis of seborrheic dermatitis. The appearance of the painful abrasions and the bullous and vesicular lesions during the past week suggested pemphigus. If the condition is pemphigus, what may be the apparent relationship between the finding of Vincent's spirillum on the skin and the clinical appearance of pemphigus? There was no Nikolsky's sign. The Pels-Macht test gave a reading of 72 per cent.

DISCUSSION

Dr. John H. Stokes: This case interested all of us at the University keenly because the staff of my office has recently seen three such cases that seem to represent transitions perhaps in a process that looks almost like one with epidemic qualities. The first case that suggested this idea did not progress to the degree of severity that the one presented has. A woman, 77 years of age, had a universal bullous eruption of pemphigoid character, particularly marked in the flexures; toward the latter part of the attack these bullae became definitely purulent; the earlier lesions arose from normal skin in the manner one sometimes sees in bullous erythema multiforme and in bullous impetigo. The gradual disappearance was characteristic of impetigo. Only at one time did the patient have a lesion in the mouth. We decided that she had had an acute septic erythema multiforme, with bullous lesions and impetigenous termination.

The next case was that of a woman who had had periodic attacks, three in the last eighteen years. In the mouth she had lesions of the type of erythema multiforme or of Vincent's angina or trench mouth with each attack, and these bullous lesions appeared on the skin. One which we saw at the time of examination was a perfectly distinct bulla arising from clear skin, which rapidly assumed

impetiginous characteristics and progressed by spreading in auto-inoculative transference over the skin, leaving hyperpigmented spots and finally clearing up after treatment with ammoniated mercury.

The third case was that of a rabbi, who, when we first saw him, looked very much as though he had seborrheic dermatitis; that is, bullous erythema multiforme, Senear-Usher syndrome and classic pemphigus were present. At the beginning his lesions were not particularly marked in the flexures, but the third time we saw him they were very marked. He had erosions over the central portion of the chest, like a moist, exudative impetigo, such as this woman presents. The bullae arising from normal skin had by the third visit become universal and purulent, and had clustered in the axillae and the flexures of the groins. Multiple paronychial and Whitlow lesions had developed on several fingers. I was also particularly interested in the presentation of this colored woman because my patient had practically identical lesions in the mouth, and strongly positive Kolmer and Kahn reactions, although he said there had been no exposure that could possibly have led to syphilitic infection—his father was also a rabbi before him, and he was of unimpeachable character. We repeated the Wassermann and Kahn tests, both strongly positive the first time, ten days afterward, and obtained much weaker positive reactions. The patient was given treatment for syphilis, although I was satisfied that the bullous eruption had nothing to do with syphilis, and his condition became distinctly worse. At the present time we are treating him for an extensive bullous impetigo, universal in extent, and we think that he exhibits an adult homologue of the pemphigoid of infants, possibly a mild streptococcic septicemic process. We have no blood cultures as yet. We shall be glad to report to this society the outcome of his case. Any one of the four diseases I mentioned might have been diagnosed when he was first seen. Now it is impossible to say what condition he has, but it looks very much as though he were suffering from a universal pyogenic infection, very possibly of vascular distribution. He has no fever, however. The false positive Wassermann reaction, if it is such, may be associated with the pyogenic septicemia; that has been known to occur.

DR. D. M. SIDLICK: The clinical picture in this case favors the diagnosis of pemphigus.

DR. F. D. WEIDMAN: When we first saw the patient we did not think of the case as one of pemphigus. Our attention was called especially to the superficial crust-covered lesions, particularly to those around the umbilicus; the pseudomembranous effect of the crusting called to my mind the cases of diphtheria of the skin described by Knowles. Vincent's organisms, not B. diphtheriae, were demonstrated in smears from the mouth and umbilicus. It was only on a later visit that we saw the blebs. In that respect, I think this case resembles those of so-called butcher's pemphigus, in which there is a rather severe toxic state, even more toxic than this woman shows, in which the bullae are simply the expression of the general toxic reaction. I therefore regard the condition in this case as pemphigus of the toxic type, possibly similar to butcher's pemphigus.

CHRONIC ERYTHEMA MULTIFORME (PSORIASIFORM). Presented by DR. FRED D. WEIDMAN.

J. S., a colored man, aged 30, from the Philadelphia General Hospital, had a widespread annular eruption of four months' duration. The distribution on the knees, back of the thighs, forearms, palms and nails and on the scalp was like that of psoriasis. The conformation and the thick adherent scale were likewise in agreement with that condition. However, the face was abundantly involved, and the scale was scarcely of laminated, silvery character. Syphilis could be eliminated, for the condition began as vesicles and the Wassermann reaction of the blood (one provocative) had been negative on four occasions. The patient had fluid in both knee joints (of four months' duration) and pain in the ankle, knee and shoulder joints; there had been a severe infection of the upper respiratory tract five months before presentation.

At the time of presentation the ensemble was very much like that of psoriasis; however, one month before there had been a tumid nodule in the lobe of the ear, and even on presentation there were still some discrete glistening nodules at the margins of the annular patches that aroused suspicions of tuberculosis. There was a definite generalized adenopathy. Indeed, the patient had been in the tuberculosis wards of the Philadelphia General Hospital on account of chronic productive cough of nineteen years' duration, but visceral tuberculosis could not be established. Biopsy, however, showed only a diffuse exudative inflammation and proliferation which was certainly not specifically granulomatous, and which suggested psoriasis in some respects.

The psoriatic features I felt were overbalanced in favor of erythema multiforme by such factors as the vesiculation at the beginning, the extreme edema of the lobe of the ear and the exceedingly discrete nodules at the margins of the patches. The acute arthritis, preceded by angina, contributed to the picture. If this conclusion were accepted, there still remained the psoriasiform features, both clinical and histologic; these aroused suspicions that the patient might have a transition case between the two that reflected something on the pathology of some cases of psoriasis. Or was this an erythema figuratum perstans in a psoriatic subject? That is, the "mixed dermatosis" concept of Brocq permits the entrance of psoriatic features, if, as and when a provocative dermatosis, in this case erythema multiforme, arises.

DISCUSSION

DR. R. L. GILMAN: I have nothing to add to the presentation of this case. At different times we considered a diagnosis of secondary syphilis, of psoriasis and, as Dr. Weidman mentioned, of erythema multiforme. At one time we thought we were dealing with a case similar to one that Dr. Weidman reported with Dr. Klauder, a generalized granulomatous eruption which later proved to be tuberculosis. In my opinion this is a case of chronic erythema multiforme.

DR. S. S. GREENBAUM: The patient states that the eruption began on the feet and ascended. It would be interesting to know whether there are any fungi in the lesions. No scrapings have been taken for fungus.

DR. D. M. SIDLICK: The type of lesion or combination of lesions that the patient presents is sharply circumscribed, having a tendency to assume gyrate formation and bilateral distribution; the patient is entirely free from itching, and the duration is four months; therefore, I think we are dealing with a case of parapsoriasis.

DR. JOHN H. STOKES: I believe that it is a fungus infection.

A CASE OF LICHEN PLANUS. Presented by DR. PILLSBURY for DR. JOHN H. STOKES.

A man, aged 21, a native of Afghanistan, who had been in this country for seven years, presented an intensely pruritic papulosquamous dermatosis. The eruption was widely scattered, being generalized, and the palms and mucous membranes were the only regions not involved. The papules varied greatly in size and had a purplish sheen, and some of them had an annular configuration. Several large scaling plaques in the scalp, both axillae and the pubic area produced atrophy with resultant partial to complete alopecia.

General examination revealed only a moderate generalized adenopathy, which was particularly noticeable in the right cervical chain, and moderate enlargement of both ulnar nerves. The Wassermann reaction was negative on three occasions. The blood count, including the differential white count, was well within normal limits. A specimen taken for biopsy from a small lesion on the back did not show any particularly distinctive changes, and we were not sure that it fully represented the changes in the process.

In Graham Little's case the alopecia occurred only on the scalp; in this case it occurred in both axillae and in the pubic area also.

DISCUSSION

DR. M. BROWN: I concur in the diagnosis of lichen planus.

DR. F. D. WEIDMAN: The extreme itching, alopecia, generalized adenopathy and the lichen planus-like appearance of the lesions recall perfectly the case I showed at the last meeting in which Hodgkin's disease had been proved histologically, and in which the lesions at times had the appearance of lichen planus. I think that some such combination as that might be present in this case, which may have as a basis early Hodgkin's disease. The diagnosis in my case was questioned by some dermatologists; this case parallels it, and, accepted as lichen planus, proves that the diagnosis in my case was correct.

DR. S. S. GREENBAUM: The lesions are of course those of lichen planus. We shall have to have a different concept of the etiology of lichen planus. One sees typical lichen planus produced by intravenous injection of arsenicals; we have seen such lesions in pseudoleukemia, and it is quite likely that in this case the etiology is different from that of the usual lichen planus that we see.

DR. J. H. STOKES: We are lucky to have this case because of the skepticism aroused at the meeting of visiting dermatologists of the American Medical Association when we showed a woman with alopecia of the Graham Little type associated with a history of lichen planus. Now we have the complete picture: lichen planus and alopecia; and the lichen planus is of such a lush and extraordinary distribution that in the future you can believe that almost any eruption is lichen planus. I agree with Dr. Greenbaum in his conception of lichen planus.

A lichenoid eruption of the lichen planus type can probably occur from a number of causes. I should be willing to add tuberculosis to the possibilities in this case, but certainly this is the clinical picture of lichen planus with extraordinarily extensive distribution. This is one of a series of three cases that we shall endeavor to report and to discuss from various angles.

A CASE OF MYCOSIS FUNGOIDES. Presented by DR. S. KATZ.

L. B., a white woman, aged 65, reported at the Graduate Hospital (Dr. Schamberg's Clinic) in July, 1931, complaining of a mass over the right side of the forehead and a number of smaller masses over the back of the neck, accompanied by itching. The patient stated that five years before a red spot appeared on the right cheek, which enlarged rapidly and was accompanied by itching, until the entire face became involved. Six months after the appearance of the first lesion she received roentgen treatment. In the course of three months she received ten roentgen treatments. She then went to another physician who gave her ten more treatments. A year and a half before presentation she received seven more roentgen treatments to the face.

Six months before, a number of small, elevated, reddish, itchy areas developed on the back of the neck, followed three months later by a large painless nodule over the right side of the forehead. At the time of presentation she had several elevated papular areas over the back of the neck, rounded, confluent and reddish. On the forehead there was a large irregular nodule, dull red and painless; also a number of scratch marks on the face where the skin was dry and somewhat atrophic. Over the corner of the right eye was a movable swelling, the size of a small marble, which appeared two months after roentgen treatment to the right side of the face. There was some light perception present. There was an ectropion of the lower eyelid.

A specimen taken for biopsy from tissue of a nodule on the forehead showed a granulomatous process, and the histologic appearance suggested mycosis fungoides. A specimen from the tissue on the back of the neck (Sept. 18, 1931) showed an inflammatory process, but did not have the appearance of mycosis fungoides.

The patient had been hospitalized at the Hahneman, Jefferson, Episcopal and Skin and Cancer Hospitals. At the time of presentation there was some itching,

but it was kept in check, she said, by a bland oil used locally. The blood count was: red blood cells, 4,310,000; white blood cells, 8,700; hemoglobin, 67 per cent; small lymphocytes, 16; polymorphonuclears, 81; eosinophils, 1; basophils, 1; abnormal cells, 2, and B. C., 1.

DISCUSSION

DR. F. D. WEIDMAN: When I first saw this case I thought it might be endothelioma capitis, but the sections certainly do not show that. I cannot get quite enough cytologic detail in the section to pass on the matter of polymorphism and some of the other much quoted characters for mycosis fungoides. I do not care to make a diagnosis on this single view of the case.

DR. JOHN H. STOKES: I think that the case is one of mycosis fungoides. It is interesting to see the anterior staphyloma. I wonder whether the patient has a lesion behind the eye; of course, there is no way of telling.

DR. S. S. GREENBAUM: I saw this patient for the first time about five years ago as a private patient. At that time she had a lichenified eczematoid area over the left side of the face, extremely pruritic, and a number of traumatic lesions. I considered the condition to be a neurodermatitis, and I treated her for a while. About two weeks before presentation, when I saw her again as a clinic patient in the Graduate Hospital, she had this lesion on her forehead. I made a diagnosis then of mycosis fungoides, as did Dr. Schamberg, and I think that the histologic picture confirms this diagnosis. It brought home to me how innocent-looking some of these premycotic lesions may be.

A CASE OF UNILATERAL SCLERODERMA WITH ZOSTERIFORM DISTRIBUTION. Presented by DR. F. D. WEIDMAN.

E. C., a Jewish woman, aged 20, presented a dermatosis that began three years before as gradually developing pigmentation, with sclerosis occurring only in the last year and slight pain beginning about four months before presentation. The dermatosis was pigmentary and macular—faint on the left side of the chest and neck and more definite over the shoulder. On the arm and forearm the macules fused into patches and were confined to the anterior and the internal surfaces. In addition, thickening and "hide-binding" were barely discernible over the chest and conspicuous on the arm. The sclerosis extended as a broad band down the arm and forearm, largely, but not completely, underlying the pigmentary portions. The deltoid was hard, almost woody.

The phases of this case were two: First, the processes were pigmentary and sclerosing, thus admitting the disease into such a loose clinical entity as scleroderma. After that, the zosteriform distribution commanded attention; the cutaneous map of the dermatosis corresponded with the distribution of members of both the cervical and the brachial plexus, the fourth, fifth and sixth cervical roots. This focused attention on these three ganglions, and of course would be useful if ramisection were eventually resorted to. Roentgenograms removed supernumerary ribs or other (opaque) pressure masses from the etiology.

We are probably dealing here with a functional disturbance of these three ganglions, essentially sympathetic, the process not being acute enough to produce the dermal lesions of zoster, but only the subacute ones of sclerosis. Since one could perceive with the hand that the diseased skin was warmer than the normal (over the right arm), Dr. B. McGlone from the physiology department made galvanometric temperature measurements, and found a difference of approximately 1 C. between the normal and the diseased arms. Tests were made for possible shifts of skin temperature under atropine and pilocarpine regimens, but they did not occur. To our surprise, however, atropine did not induce its usual physiologic effect, suggesting that the patient was in a state of vagotonia, and on this basis we have continued the atropine therapy. The patient thinks that the skin is definitely softer and the pigmentation less. Pilocarpine caused discomfort in the arm. If a response does not take place, we shall recommend sympathectomy.

because the arm is severely incapacitated; prior to that we will examine more searchingly with the x-rays to ascertain the condition immediately around the cervical roots.

DISCUSSION

DR. J. H. STOKES: This is a very interesting case, indeed, particularly the suggestions of zosteriform character in connection with it. I do not recall that the presenter mentioned what I should call marked hemiatrophy of the face, which appears in this patient. It occurs in supra-orbital herpes zoster and also in morphea of the face, neck and scalp, particularly before puberty. Cases have been reported by Osborne about 1921 or 1922. The distribution of changes in this case shows that palliative therapy does not have any startling or prolonged effects — not that I would want to say anything discouraging. Sympathectomy might be considered, but I think that there is an involvement of more than the posterior cervical roots, to judge from the configuration of the face. The mother does not show any signs of hemiatrophy, but the left side of the daughter's forehead is 2 or 3 mm. behind her right eyebrow, and the whole side of the face is "off" in this way.

DR. F. D. WEIDMAN: I had not noticed the hemiatrophy. When the patient first came to the clinic five or six months before presentation, we examined her closely for signs of sclerosis of the face. At that time I did not notice the hemiatrophy, and since then I have not paid particular attention to the face. I might say that of course this opens the question of what is and what is not scleroderma and what its scope and limitations are; a very encouraging angle has been afforded by the investigations that the Mayo Clinic is conducting, inquiries by physiologic methods into the functions of the blood vessels and nerves in the affected parts.

A CASE FOR DIAGNOSIS (PYOGENIC ULCER DUE PROBABLY TO STAPHYLOCOCCUS DERMATITIS FACTITIA?). Presented by DR. M. BROWN.

B. C., a white woman, aged 28, had an eruption that had appeared six months previous to presentation on each ankle at the same time as a small erythematous spot that increased in size, became vascular, broke down to a small ulcer and then healed, leaving a stain. We used all sorts of medication in trying to heal the lesions. They healed in the course of from ten days to two weeks, but new lesions appeared, and she had the scars of old ulcers and one active ulcer at the time of presentation.

DISCUSSION

DR. V. GARNER: I think that papulonecrotic tuberculid must be considered.

DR. S. S. GREENBAUM: I agree that papulonecrotic tuberculid would have to be considered, but at least one lesion that the patient presents is not a nodule at all, and it has never been one. The eruption is symmetrical, and its appearance suggests a factitial origin.

DR. M. MARKOWITZ: It might be due to some drug or hydrochloric acid, thus being factitial.

DR. J. H. STOKES: I considered a factitial lesion, but the voice, face and manner of the woman did not suggest this at all. I should be inclined to say that this is a tuberculid. She is the type that might have a tuberculid or possibly one of the localized infections beginning around the follicle, a small necrotic ulcer, which I used to call septid and wonder if the distribution could be vascular.

DR. M. BROWN: As far as a tuberculid is concerned, as the lesion leaves the erythematous stage it becomes vesicular and pustular and then breaks down. At first we thought the lesion a pyogenic ulcer, and as the condition continued we began to believe that it was dermatitis factitia. As Dr. Stokes mentioned, the patient is not the type to have a factitial lesion. She is employed, is not married, and is free from any domestic difficulties; there is nothing about the family history to suggest a factitial type of lesion, yet the ulcer heals quickly — in ten days it is

fully healed — and then a new one appears. The erythematous spot does suggest friction, such as frost-bite, due to rubbing of the part. This is the first time that I have seen the beginning of the eruption suggest that it is a factitial type.

A Case of Mild Darier's Disease. Presented by Dr. M. Brown.

B. M., a man, aged 35, presented small papules that seemed to be centered around the follicles, of six years' duration. The lesions were dark brown. He had had about half a dozen roentgen treatments, which had flattened down the lesions considerably.

DISCUSSION

Dr. D. M. Sidlick: I subscribe to the diagnosis of Darier's disease. I agree with Dr. Brown that the lesions have shown considerable improvement since the first time I saw the patient.

Dr. John H. Stokes: I can only say that the case puzzles me. In my recollection of Darier's disease, the papules are much coarser, the follicular character is much more marked, and the lesions are conspicuous around the axillary folds; this may be Darier's disease, but I should not give that first consideration. At first glance I thought the patient had multiple verrucae; the papular lesions look like verrucae, but I cannot say what it is.

Dr. F. D. Weidman: I think that this case requires a biopsy. When I first saw the patient I thought he had pityriasis rubra pilaris. For Darier's disease these lesions are rather uniformly spaced. The pigmentation and infiltration are classic for pityriasis rubra pilaris. The condition may be an interesting link between pityriasis rubra pilaris and Darier's disease and perhaps some other infection.

Dr. S. S. Greenbaum: If this is a case of dyskeratosis follicularis, it is certainly one of the abortive or larval types developing late in life. There has been but one case shown before this Society in the past fifteen years, and that was shown by Dr. Stellwagon, a much more extensive case. If the case is not keratosis follicularis, I do not know how to diagnose it.

Dr. M. Brown: I presented this case as a mild case of keratosis follicularis. Dr. Stokes' conception of the disease is the fully developed, severe case, of which I have seen but one in all the time I have been coming to these meetings. Almost the exact shade and involvement of the follicles found in the case presented are given in the classic description, so I still consider it a mild case of keratosis follicularis. The follicles have flattened down considerably as a result of roentgen treatments, six quarter skin units.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

Leo Spiegel, M.D., *Secretary*

Regular Meeting, Oct. 6, 1931

Joseph J. Eller, M.D., *Chairman, Presiding*

A Case for Diagnosis (Lupus Erythematosus Disseminatus?). Presented by Dr. Eugene Traub.

A boy, aged 19, first came under observation a year prior to presentation. He had been working for about a year as a printer, handling type, benzine and alcohol. To clean his hands he had used grease solvent, and he noticed that his hands became red. Six months before being seen by the presenter, the

patient had noticed black spots on his palms; these were hard to the touch and occasionally itchy. He would attempt to dig at them with a knife or with the edge of a razor blade from time to time. Three months later he first noticed redness and scaliness on the back of the knuckles and the interphalangeal joints of both hands and on both elbows. There was slight redness of the face beneath both eyes; this had been present for the six months prior to presentation, with scaliness and redness of both ears for the same length of time. For the past few months he had also noticed a weakness in the grip of both hands, a swelling of the proximal thirds of the second, third and fourth fingers of both hands, and a thinning of the interosseous areas, notably between the first and second fingers.

In September, 1930, there were scattered over the palmar aspect of both hands numerous lesions varying from 1 to 3 cm. in diameter. The smaller lesions were brownish black, slightly raised over the surface of the skin, hard to the touch and surrounded by a zone of erythema from 1 to 2 mm. wide. The larger lesions had a central depressed area, often covered with a brownish crust or scale and surrounded by a zone of erythema. Over the tips of the fingers the skin was thinned and fissured, with numerous depressed areas. Over the dorsum of the interphalangeal joints were reddish, scaly lesions, with occasional pinpoint, brownish, hard areas similar to those on the palm. There were reddish scaly areas on both elbows, the outer aspect of both ears and beneath the inner angles of both eyes.

The urine was examined for lead and arsenic, but none was found. Specimens were taken for biopsy from the dorsal and palmar lesions and the areas on the elbows. Clinically, the pinpoint, hard areas appeared to be present in the orifices of the sweat ducts. A clinical diagnosis of porokeratosis was therefore tentatively made. Section showed that the brownish, hard areas were due to downgrowths of hornified epithelium which flattened the rete cells so that in some places the latter were only two or three cells high. Around these areas was a round cell infiltration. The blood vessels in the papillary layer and midcorium were dilated and surrounded by a round cell infiltration. The lesion from the area of the elbow showed merely dilatation of the superficial capillaries and a round cell infiltration, chiefly vascular.

Because of the microscopic observations, the diagnosis of punctate keratoderma was considered. This, however, did not explain the other features of the case, namely, the muscular weakness and the scaly red areas found commonly in cases of heavy metal intoxication.

The patient disappeared from the dispensary and was not seen again until Oct. 2, 1931. At that time he presented a totally different picture. He had in the interim been a patient at the Mount Sinai Hospital, where he had suffered with fever for quite a time. Several specimens, including the removal of two lymph nodes, were taken for biopsy. The urine was found to contain lead. The diagnosis of lupus erythematosus disseminatus was made.

On October 2, the patient was in a much poorer physical condition than a year previously. He was much thinner and could climb stairs only with difficulty. For the last two weeks he had had numerous hemorrhages from the mouth. The clinical picture was now dominated by two features, e. g., atrophy and hemorrhage. There were no longer the pinpoint, hard, brownish areas previously observed. In their place were reddish areas of atrophy, many with numerous scattered petechial hemorrhages. Similar atrophic and occasional hemorrhagic areas were present on the backs of the hands, over the elbows and on the back of the shoulders. There was a subungual hemorrhage of the right second finger. The mouth showed numerous hemorrhages on the tongue, cheeks and soft and hard palates, and in addition the anterior third of the tongue showed distinct atrophy. There was also an area of pigmentation on the nose and adjacent cheek areas in the shape of a butterfly.

Physical examination gave negative results except for dilated pupils, a few scattered râles throughout the lungs and slightly exaggerated reflexes.

The Wassermann reaction of the blood was negative. Examination of the blood showed: 3,650,000 red cells, 55 per cent hemoglobin, 4 per cent mononu-

clears, 8,000 white cells, 75 per cent polymorphonuclears and 22 per cent lymphocytes. The coagulation time was five minutes, and blood platelets numbered 299,000.

Chemical analysis of the blood showed: 16.5 per cent urea nitrogen, 1.3 per cent uric acid, 76.4 per cent sugar and 454.3 per cent chloride. Urinalysis showed no arsenic or lead.

Biopsy of a section showed a persistence of the elastica throughout the whole tissue. A hematoxylin stain showed an epidermis that was acanthotic, with several horny plugs at the follicle openings. There was a peculiar lamellation of the horny layer, which was very much thickened. The blood vessels were dilated and surrounded by a moderate cellular exudate.

DISCUSSION

DR. EUGENE TRAUB: There were many reasons for presenting this unusual and interesting case. The patient has been quite thoroughly studied both in our hospital and at the Mount Sinai Hospital. No one has been able to arrive at a diagnosis that will satisfy the entire picture. He has been presented at various dermatologic societies, first with the diagnosis of porokeratosis Mibelli, and subsequently with a diagnosis of disseminated lupus erythematosus. On watching this man over a period of a year, with the exception of a few months while he was at Mount Sinai Hospital, we noted an eruption that began at first as tiny punctate hyperkeratoses with a central depression surrounded by a faint zone of erythema. Very little, if any, atrophy is present at this time. As the disease has progressed, these slightly warty or horny processes have gradually disappeared, especially the ones on the hands, elbows and tip of the ear, to be repeated by a superficial atrophy and bluish discoloration, apparently circulatory in origin. The lesions on the face at the onset were not characteristic of any special dermatosis. There were a little scaling and the faintest erythema. These have now resulted in a questionable atrophy, but a definite pigmentation on both cheeks. The patient's general health has been materially impaired from the onset. A swelling of the proximal thirds of the fingers with a thinning of the interosseous areas and a weakness of the grip of both hands are noted. The patient has also lost over 50 pounds (22.7 Kg.) in a period of a year. A late feature of the disease is the striking appearance of the tongue, which shows a smooth atrophy and evidence of hemorrhage. There are also subungual hemorrhages. The patient's occupation as a printer, handling type, benzine, alcohol, etc., led us to believe that he might have a metal poisoning.

Our examinations for lead and arsenic, however, have been negative. I understand that lead was found in the urine at Mount Sinai Hospital. Whether this is the case or not, and in the face of an otherwise negative medical examination, the entire picture seems that of a subacute or chronic toxemia. Therefore, it would be proper to classify this as a medical case with unusual skin manifestations.

DR. LOUIS CHARGIN: This patient was presented before another society about six months ago with the diagnosis of porokeratosis Mibelli. Although I have never seen a case of this disease, I knew from the description in textbooks that it did not fit in with the picture presented. This patient presents an eruption that is for the most part over the flush areas of the face, on the ears, palms and finger tips and over the dorsal aspect of the flexures of the fingers. It is erythematous, somewhat scaly here and there, and on the ears, as well as on the fingers, shows definite atrophy.

The picture is one of lupus erythematosus of the disseminated variety. The patient also has lesions on the mucous membranes of the cheeks, also a part of the disease. The atrophy of the hands I cannot account for.

Because a diagnosis of porokeratosis was made by confrères, I thought it well to study the case further and had the patient admitted to Mount Sinai Hospital, where he was carefully studied. After complete physical and laboratory studies, including biopsies, the diagnosis of lupus erythematosus was agreed on.

DR. BOLESLAW LAPOWSKI: This is not, in my opinion, a case of lupus erythematosus, owing to: first, the absence of scars; second, the presence of muscular atrophy of the fingers, especially between the right thumb and index finger with normal macroscopic skin, and third, the peculiar aspect of the round, erythematous, dark brown, not infiltrated spots of the tongue, which in lupus erythematosus of the mucous membranes and skin of such duration as in this patient would leave scars on the face, which are not present.

Further study is required to make the diagnosis, and a detailed knowledge of what has been done and what medicines this patient has received up to the present is necessary.

DR. ISIDORE ROSEN: The case is not unusual. We occasionally see cases of disseminated lupus erythematosus with involvement of the hands and lesions elsewhere on the body. The patient's ears present erythematous and follicular lesions, and one or two areas in the scalp show similar involvement. The lesions in the mouth are interesting and are also occasionally seen in conjunction with this particular type of lupus erythematosus. On account of the softness of the tissue and traumatism by the ingestion of food and mastication, the lesions are not typical in appearance. It is possible that this type has associated with it, as Dr. Traub mentioned, some pathologic active cardiovascular disturbance.

DR. WALTER J. HIGHMAN: I think that it is difficult to apply the proper label to a case of this sort. It seems to present some clinical and histologic manifestations susceptible to the appellation of lupus erythematosus rather than to any other. Whether that is making a diagnosis, I do not know, nor do I know whether the edema in the lesions, which Dr. Traub has called attention to, and the follicular hyperkeratosis and telangiectasis in the area involved, with suggestive changes in the epidermis, are sufficient to confirm the conception of lupus erythematosus. As to the hemorrhages in the mouth, they may or may not have something to do with the general condition. Patients with lupus erythematosus may have some other disturbance.

DR. HERMAN GOODMAN: I saw the patient about three months ago. At that time he presented no lesions such as he shows now. His chief complaint was the lesions on the palms. I was satisfied then that he had a parakeratosis with lysis, as the lesions showed punctate hyperkeratosis with central depressions. Although many sections were examined, no positive diagnosis could be agreed on. Dr. Monash saw the patient and reviewed the findings. I ask that he be invited to say a few words regarding this patient.

DR. SAMUEL MONASH (by invitation): I only wish to emphasize the fact that when the patient first presented himself the lesions bore no resemblance to those seen here. The atrophic lesions now present on the hands are the end-result of the numerous brownish-black, punctate, hyperkeratotic lesions originally seen, which microscopically resembled keratoderma punctata. Although at the present time a diagnosis of lupus erythematosus disseminatus seems not unlikely, it would not even have been considered a year ago.

DR. OSCAR LEVIN: Clinically, the patient presents lesions typical of disseminated lupus erythematosus. Scattered over the face, trunk and other parts of the skin are purpura, telangiectases, erythema, superficial atrophy and a slight pigmentation of the face from the absorption of old lesions. There are evidences of a general disease, as shown by marked anemia, loss of weight, purpura of the gums and lesions of the tongue suggestive of lupus erythematosus. There is also a condition of the upper extremities manifested as an edematous, scleroderma-like infiltration. The cutaneous condition suggests to me what has been previously noted as occurring in a severe type of disseminated lupus erythematosus. These cases probably belong to a group in which toxins act on the small blood vessels, producing what has been described as capillary toxicosis. These cases have been studied, and it has been found that the heart, kidneys and even the liver may be implicated. Among the cases that have been observed during the

past few years, the patients have tended to lose weight and strength, and death has often occurred from bronchopneumonia.

DR. LOUIS CHARGIN: This patient was studied by the medical service at the hospital by various members of the staff, including special consultants, and no light could be thrown on the etiology; nor could we account for the atrophy of the hands. With respect to lupus erythematosus and atrophy, I think that it is well recognized that many cases clear up without the slightest trace of atrophy, especially the acute, subacute and disseminated varieties.

DR. WALTER J. HIGHMAN: I believe there is divergence of opinion among the various speakers referable to the fact that if we talk about lupus erythematosus at all, we must mean one of its classic pictures, whether lupus erythematosus disseminatus or lupus erythematosus discoides. It is obviously not necessarily a hyperkeratotic process, when the condition that is being discussed happens to be that of lupus erythematosus disseminatus. This would obviously be a capillary disease, as Dr. Levin pointed out. The form of lupus erythematosus known as the discoid type is not only a capillary disease, but a disease of the epidermis, so far as manifest changes in this tissue are concerned. It does not follow that because the capillaries are involved in the process the epidermis must be. The present case is curious. This patient has manifestations of disseminated lupus erythematosus and also manifestations of that form of lupus erythematosus which involves the epiderm, so that hyperkeratotic plugs are formed. Whether the entire concept of lupus erythematosus as originally expounded by the Viennese school (and subscribed to by us, to date) will hold, I do not know. No one else knows. This case has unusual manifestations, whether it be lupus erythematosus or not.

LUPUS MILIARIS IN A SYPHILITIC PATIENT. Presented by DR. DAVID BLOOM.

G. H., a woman, aged 29, came to the clinic of the Bellevue Hospital in April, 1931, with a generalized eruption and a 4 plus Wassermann reaction. She received thereafter one course of neoarsphenamine and mercury followed by a course of bismuth. While under antisyphilitic treatment, the patient noticed, in May, the present eruption, which started on the back of the neck and gradually became generalized. The eruption consisted of pinhead to small pea sized, shiny, flat, skin-colored papules, some slightly reddish, others more yellowish, located on the trunk, but closely aggregated on the back of the neck. There were a few papules on the hands.

A guinea-pig inoculation made four weeks prior to presentation was still negative. The Mantoux test likewise gave negative results. Histologic examination showed typical tubercles with epithelioid and giant cells. A roentgenogram of the lungs showed no signs of tuberculosis. The last Wassermann test, made in June, gave a negative reaction.

DISCUSSION

DR. GEORGE C. ANDREWS: I do not think that there is enough evidence as yet to prove that this case is one of lupus. Clinically, the condition has not the appearance of lupus to me. Some lesions have spontaneously disappeared from the arm without scarring. Although the microscopic observations were said to be typical of tuberculosis, I would certainly like to see the slide myself before accepting the diagnosis.

DR. FRED WISE: I think that this is one of the most interesting cases presented at the meeting, and I am sure we would be interested to learn the result of further investigations, as well as the outcome of the animal inoculations, tuberculin tests, etc.

DR. SAMUEL PECK: Lupus miliaris is one of the few tuberculous lesions of the skin that shows typical tubercle formation. Guinea-pig inoculation is, of course, the best proof of the tuberculous nature of a lesion when it is positive. However, it is well known that even in cases in which tubercle bacilli have been

found on section from cases of lupus miliaris guinea-pig inoculations can be negative. One of the most important diagnostic measures in these cases is a tuberculin reaction, which has a tendency to be negative in this disease. This negative reaction has been called positive anergy by Jadassohn. Therefore, a negative tuberculin reaction in a lesion that clinically and histologically speaks for lupus miliaris is of great aid in the diagnosis.

I reported three cases of lupus miliaris with negative tuberculin reactions. In one of these cases I was able to demonstrate tubercle bacilli by guinea-pig inoculations. I was able to gather about a hundred cases of lupus miliaris from the literature of the world in which the reaction had been determined, and the statement first made by Jadassohn about twenty years ago that these cases have a tendency to a negative tuberculin reaction was substantiated.

DR. PAUL GROSS: Assuming that this is a case of lupus miliaris, I think that it should be called lupus miliaris disseminatus facei, a condition that usually involves the face and leaves the body free. For miliary lupus vulgaris, the patient surely does not appear ill enough, and the eruption is not characteristic. We know that syphilis and leprosy may in rare instances give a typical tuberculous structure. In view of the positive Wassermann reaction, I would be led to believe that this is a case of tuberculoid syphilis.

DR. DAVID BLOOM: I have not much to add. This case is interesting because the eruption appeared while the patient was under antisyphilitic treatment. We thought that the negative Mantoux reaction might possibly be due to the syphilitic infection, which lowered the forces of the organism and changed the positive reaction to a negative one. We are going to follow up the results of the guinea-pig inoculation.

A CASE FOR DIAGNOSIS (RHINOSCLEROMA?). Presented by DR. FRED WISE.

B., a man, aged 31, from the New York Post-Graduate Hospital, came from Barbados and had been sent to the United States by Dr. C. H. St. John with the report that the patient's lesions had been present for six years. In spite of a negative Wassermann reaction, a diagnosis of syphilis had been made and the patient was given antisyphilitic treatment, with no beneficial results. The ingestion of potassium iodide increased the ulceration and had to be discontinued. A curettement of the nose and faucial pillars resulted in improvement of the nasal condition only. The patient entered the Post-Graduate Hospital Skin Clinic in July, 1931. The diagnoses considered were: rhinoscleroma, syphilis, tuberculosis and gangosa.

Wassermann and Klein tests were done and were reported as negative; a specimen was taken from the fauces for biopsy, and the report was a chronic purulent inflammation with plasma cell infiltration and no evidence of malignancy. A piece of tissue was used for guinea-pig inoculation; the animal lost no weight, and when the guinea-pig was autopsied, the glands and organs were found negative for tuberculosis. A roentgenogram of the thorax revealed hypervascularization of both upper lobes and emphysema of both lower lobes. Examination of the exudate from the palate for ameba was negative, but despite this, fifteen injections of emetine hydrochloride were given, with no beneficial results. Smears taken from the ulcerated areas showed many pus and red blood cells, occasional cocci, no Donovan bodies, no lepra bacilli and a gram-negative rod of the Friedlander group, which did not give a typical reaction of the Frisch bacillus in sugar mediums.

The patient was examined by Dr. J. A. O'Connor of the Presbyterian Hospital, and he reported the case as a "probable rhinoscleroma," although he was also unable to demonstrate the Frisch bacillus. The complement fixation test for the Frisch bacillus was negative.

On the soft palate and encroaching on a small portion of the hard palate, extending laterally to the commissures of the jaws and involving the uvula, faucial

pillars and arch of the pharynx, there was a series of ulcerated lesions formed by discrete and coalesced ulcers with raised, indurated edges. The entire area was infiltrated and hard to the touch. The posterior nares and also the floor of the posterior portion of the nose were involved in the process. The lesions were not painful.

SUBSEQUENT NOTE.—Subsequent treatment with radium caused the lesions to heal almost completely within six weeks. The diagnosis of rhinoscleroma was accepted by several rhinolaryngologists.

DISCUSSION

DR. ELIAS ABRAMOWITZ: This patient appeared at the Post-Graduate Clinic, also, in Dr. Rosen's service. Syphilis and tuberculosis were excluded. We thought that we might be dealing with a case of gangosa. The biopsy gave the first clue pointing to rhinoscleroma, even though the Frisch bacillus was not found. We decided to use antimony and potassium tartrate and emetine on the assumption that the patient might have some tropical ulceration. There was no improvement following this therapy. The patient seems to have made considerable progress for the better since the application of radium, and I would construe this as favoring the diagnosis of rhinoscleroma.

DR. GEORGE C. ANDREWS: This case is so unusual that it is difficult to make a positive diagnosis without more study. However, I should like to call Dr. Wise's attention to an article by Escomel (*Rev. med.-panamericana* **4**:189 [April] 1929) on the types of American leishmaniasis. There is a form of espundia that affects the palate with lesions which fit closely to those of this patient, known as the "palatal cross of espundia." I think that espundia should be strongly considered as a possible diagnosis and that injections of antimony and potassium tartrate should be given persistently. The patient has had only five injections of antimony and potassium tartrate, and these were given a long time ago. It would probably take months of such treatment to show any clinical improvement.

I do not think that the case is one of rhinoscleroma. The bacillus of rhinoscleroma is usually easy to find, and the serum of the patient could be sent to the Army Medical School for complement fixation tests with the Frisch bacillus. My impression is that one does not see the little ulcerations that are present in this case in rhinoscleroma.

DR. HOWARD FOX: Dr. Andrews suggested the possibility of leishmaniasis. I would first like to call his attention to the fact that the organisms of this disease are not the Donovan bodies, which are generally agreed to be the cause of granuloma inguinale. Of the three types of leishmaniasis, the one that is endemic in the Americas differs from both kala-azar and Oriental sore. Leishmania braziliensis is probably the best name for the American organism. I also object to the use of the term espundia, which is merely a local name in Peru for a disease that occurs in Mexico, Central America and nearly every country in South America. The disease is spoken of in Brazil as nasopharyngeal leishmaniasis, as in a certain percentage of cases the mucous membranes of the nose and throat are eventually affected. No one in Brazil uses the local term espundia.

When the mucous membranes are involved, the disease appears first in the nose, which is often severely deformed, as shown in my recently published photographs. Later the pharynx may be affected. I doubt whether a localized lesion of the pharynx could occur without previous involvement of the nose. Many of these cases give a history or show scars of cutaneous lesions, often preceding the ones in the mucosa by many years. It would be proper in this case to search for Leishmania in the lesions in both the nose and the throat.

DR. GEORGE C. ANDREWS: I understand that there are two types of South American leishmania that cause chronic ulcerative rhinopharyngitis. Following the primary sore, or chancre, on the skin, there may be a direct extension to the mucous membranes by which the disease extends peripherally from the chancre

without any breach of continuity. This variety is the one mentioned by Dr. Fox and, I think, is referred to as uta. The second variety, called espundia, has a different course of development. After the espundic chancre, a variable period free from symptoms occurs. Sometimes this period is very long, and the infection is present only as a constitutional disease, like syphilis. After a long, latent period tertiary lesions appear on the nasopharynx and form a destructive and mutilating process. In some of these cases the ulcerations on the palate form deep furrows that cross one another, as on the palate of this patient.

DR. HERMAN GOODMAN: We have gone far afield. The question is whether this patient should be regarded as requiring treatment for rhinoscleroma. A review of the facts shows: The patient is a foreigner; he had a hard lesion of the palate, and some improvement was noted after the application of roentgen rays or radium. The pathologic and bacteriologic examinations were not conclusive. This does not lead to the diagnosis of rhinoscleroma. Foreigners with this affliction come to our shores from Russia rather than from South America. The hardness is part of many other lesions. The improvement following treatment with radium cannot be used as proof in favor of rhinoscleroma. I think that the suggestion of tropical or near tropical disease is much more in order than that of rhinoscleroma. The resemblance between granuloma inguinale, for example, and rhinoscleroma may be so great as to lead to the conclusion that they are the same disease. Randel of Philadelphia attempted to prove them to be the same. The antimony and potassium tartrate used in this patient should be checked, if the best results are to be obtained. If the solution is sterilized by autoclaving, the double salt is destroyed and its efficacy for granuloma inguinale is lost. Failure to improve granuloma inguinale may be traced to commercial solutions so prepared. I have always made up the solution with antimony and potassium tartrate powder and freshly distilled, sterilized water.

ACANTHOSIS NIGRICANS. Presented by DR. PAUL GROSS.

J. S., a Jewish woman, aged 66, married, was admitted to the medical service of the Presbyterian Hospital on Sept. 28, 1931, complaining of loss of 34 pounds (15.4 Kg.) during the past year and pallor and weakness of three months' duration. About a year prior to presentation marked itching had developed on the arms, breasts, axillae and perineum. There was no rash, and chrysarobin was prescribed for three weeks. Since that time the same areas had become a deep brown, with a rather thickened, roughened skin. She had also noted a number of small moles scattered over her face, chest and hands which she was sure she had never had before this time. At the onset of her illness she had had from eight to nine formed bowel movements a day, and at the time of presentation the bowels moved three times a day. There was no history of bleeding. The patient had also had a peculiar stinging, shriveling sensation in the tongue for the past six months, with small raw areas on the roof of the mouth and an intermittent loss of taste. Four months prior to presentation the patient had noted hair falling from the arms and axillae, and then the hair of the scalp had begun to fall until there was complete alopecia.

Examination showed a strikingly symmetrical, pigmented, thickened skin in the axillae, the inframammary areas, on one third of the abdomen, in the inguinal, gluteal and perineal folds and along the dorsal and lumbar vertebrae. These areas varied in color from café au lait to tan and grayish brown. The more recently involved areas were roughened and inelastic; the skin markings were exaggerated, similar in appearance to the bark of a tree. In addition to these characteristics, the old lesions in the axillae and perineal folds were covered with soft, smooth, linear, filiform papillomas. The palms, and to a slight extent the soles, were covered with smooth, inelastic epithelium. The skin of the hands appeared "too large for them" and had a velvety feel. On the dorsum of the right hand and on the left side of the forehead were two hyperkeratotic tumors, 1 cm. in diameter.

All of the teeth were missing. The tongue was moderately fissured and had a few filiform papillomas on the middle third. The edges were smooth. The hard palate was slightly shriveled, and there were a few fine granulations. There was no pigmentation.

The scalp was covered with a fine new short growth of black and gray hair. The hairs in the axillae and along the forearms were very scant. There had been no change in the hypertrichosis of the chin. The nails were normal.

The blood count showed 20,160 white cells and 48 per cent hemoglobin. The Wassermann reaction was negative. The sugar content of the blood was 1.2 Gm. The basal metabolic rate was 7 plus. A guaiac test of the stool gave a 4 plus reaction (on three examinations).

Roentgen examination of the skeleton showed no evidence of bone destruction; the chest was normal, with the exception of calcification of the abdominal aorta. Three gastro-intestinal series showed the colon to be normal, and the remaining films were to be reported on at the time of presentation.

The biopsy report was not ready.

DISCUSSION

DR. HOWARD FOX: This case is especially interesting to me as I saw her as a private patient two years ago. There was nothing at that time remotely to suggest acanthosis nigricans, excepting possibly the location. There was no appreciable pigmentation or rugose elevations, and the patient was in apparent good health.

DR. SIGMUND POLLITZER: This is a perfectly good case of acanthosis nigricans. The localization, the soft rugose thickening in the region affected and, what Dr. Hopkins told me privately (not recorded in the history), roentgen evidence of a tumor in the epigastric region make a complete chain of events that leaves no doubt as to the character of the disease. The patient has carcinoma with the skin lesions of acanthosis nigricans. The lesions are well distributed in the typical regions: back of the neck, in the axillae, slightly in the bend of the elbows and in the inguinal region, the anal region and the intragluteal fold. The skin in these regions is thickened and pigmented. The palms have a peculiar soft thickening; the mouth shows doubtful changes; the dental plate may not fit perfectly, and the tongue shows a slight surface thickening. Altogether, I would say that this is a perfectly characteristic picture of acanthosis nigricans.

DR. ADOLPH ROSTENBERG: This woman shows a few warty excrescences on the chest which are characteristic of acanthosis nigricans. I observed a similar case in an elderly man in whom a crop of such verrucae developed rather suddenly in uncommon locations, like the chest and forearms. He also had roughening and deep discoloration of the axillary and inguinal regions and dark pigmentation of the neck. The question of a carcinoma of the stomach was raised. He died, and a carcinoma of the wall of the stomach was found at autopsy.

DR. PAUL GROSS: It is a real privilege to present a case of acanthosis nigricans in the presence of Dr. Pollitzer. This case demonstrates that dermatologists will have something to offer the internist. When we were called to see this patient, we rather surprised the medical man by our assurance that the patient probably had a malignant tumor of the abdomen. This had been suspected on the basis of a guaiac test of the stools, but the definite diagnosis was made by roentgen examination only after we stressed the point. I would like to ask Dr. Pollitzer whether the warty lesions are commonly seen in acanthosis nigricans.

DR. SIGMUND POLLITZER: The lesions are seen in a small percentage of cases. I do not think that they are characteristic. Willy Meyer, the surgeon, some years ago grouped a number of these cases together and recorded them as evidence of acanthosis nigricans, an abortive type. I do not quite agree with him, however. The same sort of lesions is not infrequent in elderly people who show no sign of acanthosis nigricans or of an abdominal cancer.

PEMPHIGUS VULGARIS. Presented by DR. GEORGE C. ANDREWS.

W. Z., a man, aged 68, an Austrian, came to the Memorial Hospital in September, 1931, with leukoplakia of the tongue and marked glossitis. He also had a skin eruption, and was referred to the Vanderbilt Clinic. The history from the beginning was as follows: About seven months prior to presentation, a sore developed on the lip, which was treated at a New York clinic by electrocoagulation. A few weeks later hoarseness developed, whereupon treatment with radium was suggested; the patient received two treatments, and no improvement resulted. Again the lesion on the tongue was removed. The patient complained of difficulty in eating, and was sent to the Memorial Hospital for treatment with radium. There the teeth were removed, and magnesium sulphate was prescribed internally and sodium bicarbonate as a mouth wash. Then the lip became sore, and shortly thereafter the lesions appeared on the skin. The patient had been in good health except for mild diabetes.

Physical examination showed numerous erosions and ulcerations of the tongue. The inner surface of the lips and cheeks near the angles of the mouth was partly covered by whitish hypertrophic membranes. There was a distinct hoarseness, but an examination of the larynx was not made. On the lips and chin were heavy crusts suggesting dried bullae. In the jugular and nasal regions there were a few dried pustules. The feet presented bullae and scaly areas.

DISCUSSION

DR. FRED WISE: The interesting point about this patient is that he appeared at the Post-Graduate Hospital six months ago with a lesion of the tongue alone. Two specimens were taken for biopsy with three months intervening, and the findings showed unmistakable squamous cell carcinoma. The patient went to a radium expert, who gave him treatment. After extraction of his teeth, pemphigoid lesions appeared. Here is a patient with a probable carcinoma of the tongue in whom pemphigoid lesions developed after extraction of the teeth and treatment with radium.

DR. CHARLES WOLF: I should like to discuss this case in conjunction with the other case from the Vanderbilt Clinic (that presented by Dr. Gross). This patient was treated with radium in May, 1931. The other patient was also treated in May. The first patient had leukoplakia, and biopsy showed simple inflammation. Two or three weeks after treatment with radium, an eruption appeared in the mouth, which the French call "epithelitis," a reaction following radium. Coutard stated that deep roentgen treatments that are administered daily for the purpose of destroying maturing malignant cells produce an "epithelitis" of the mucous membranes. Perhaps the eruptions on the buccal mucosa in these two cases may be a reaction to radium, and the bullous eruption on the body may be a toxic erythema bullosum. The same thing applies to the case reported by Dr. Gross. We have to see more of these cases in order to determine the relationship to the treatment with radium.

DR. WALTER JAMES HIGHMAN: Pemphigus, after all, in its incipient stage is not a condition that can be recognized with absolute certainty, but one that can only be suspected. The well known fact Dr. Wise alluded to, namely, that pemphigus often starts in the mouth after dental treatment, is, like all well known facts, generalized, and is based on nothing more than an impression. Everyone has dentistry done. In those cases of pemphigus of the mouth in which there has been dental interference, one is led to think that the dentist may have provoked the disease. As with menstruation that occurs regularly in short cycles, it is often assumed that a disease may have some relation to the phenomenon, the relationship actually being only one of time. Pemphigus can never be recognized until it is pemphigus, and although diffuse lesions in the mouth make one strongly suspect pemphigus, I do not believe a certain early diagnosis can be made. I think it is just as likely that these patients may have pemphigus as not.

DR. GEORGE C. ANDREWS: This patient had lesions not alone in the mouth, but also on the face, the genitals and the toes. This localization is characteristic of pemphigus. He was under the care of physicians at the Memorial Hospital for several weeks, and during that time, after observation and microscopic examination, they decided that he did not have cancer of the tongue. In spite of the biopsy mentioned by Dr. Wise, the pemphigus is at this time of supreme importance. If he recovers from the pemphigus sufficiently, I will send him back to the Memorial Hospital with the report of the biopsy as mentioned by Dr. Wise.

MULTIPLE EPITHELIOMAS (ARSENICAL?). Presented by DR. GEORGE C. ANDREWS.

E. F., a woman, aged 75, single, born in Germany, had had the condition for forty years. She gave a history of taking solution of potassium arsenite when 15 years of age for eczema, and she had taken it subsequently of her own accord, but did not remember for how long or in what dosage.

Examination showed palm-sized and smaller lesions, mostly on the back, but also on the chest and thighs; these were flat infiltrations of a firm, waxy consistency, and appeared to be basal cell epitheliomas. Histologic examination of one lesion from the back showed a neoplastic infiltration of the corium with groups of spindle cells with relatively large vesicular nuclei and little cytoplasm. Many mitoses in all stages of development were noted. These masses of epithelial cells varied considerably in size and apparently arose from multiple foci. In several areas the cells showed prickle cell characteristics. There was a massive infiltration of the corium with numerous plasma cells. The histologic diagnosis was multicentric basal cell epithelioma.

The Wassermann reaction was negative. The arsenical content of the tissue and blood was examined, and an attempt was made to stain the tissue for arsenic deposits, with the following results: before the injection of thiosulphate, 0.065 mg. of arsenic per hundred grams of solid; after the injection of thiosulphate, 0.108 mg. of arsenic per hundred grams of solid (Sept. 10, 1931).

DISCUSSION

DR. HOWARD FOX: I think that every one would agree with the diagnosis of multiple epithelioma of the superficial type, though I do not think that any one could prove that this was due to arsenic.

DR. GEORGE C. ANDREWS: One frequently encounters patients with epitheliomas who give the history of having taken or having been exposed to arsenic. These histories may suggest that the epitheliomas are due to arsenic, but it is another matter to prove this point. We are attempting to do so in this case, by examining an excised epithelioma for arsenic deposits. I hope that other members of the section will attempt to prove the relationship in similar cases that come to their attention.

One of my patients had been treated with arsenic for psoriasis, and she had multiple epitheliomas. After removing the lesions, I gave her sodium thiosulphate by mouth for about two years, and since then no new epitheliomas have developed. It seemed to me that in this instance sodium thiosulphate had a good effect, because before the patient took it new epitheliomas appeared every few months.

DR. HERMAN GOODMAN: In the days before the roentgen rays, carcinoma on the basis of pre-existent psoriasis was known. The cases were divided as pure carcinoma psoriasis and arsenic carcinoma. Arthur Alexander assembled eighteen such cases. Of these, eleven were considered as malignant degeneration of arsenic hyperkeratosis, or arsenical carcinomas on psoriasis, and the remaining seven as pure psoriasis carcinoma. I have recently reported the case of a woman with about 120 square inches of roentgen carcinoma on psoriatic areas.

A Case for Diagnosis (Lupus Vulgaris; Syphilis?). Presented by Dr. Paul Gross.

E. F., a colored woman, was admitted to the Vanderbilt Clinic on Sept. 16, 1931. The patient gave a history of tonsillectomy at the age of 16. Four years prior to presentation her tonsils were again operated on, and at about the same time a condition developed in the nose. At that time a blood test was made, and ten intravenous injections were given without improvement of the condition. For one year thereafter, there had been hoarseness. The patient lost 50 pounds (22.7 Kg.) during the three years prior to presentation. More recent treatment consisted of roentgen therapy.

On examination, an eruption was found involving most of the nose, which, especially on the margins, showed brownish-red nodules of soft consistency. On the left ala nasi was a nodule about the size of a hazelnut and fairly soft in consistency, with a smooth surface. There was a scar on the left side of the soft palate, and the uvula was drawn over to the right. To the left side of the uvula there was a group of small reddish papules.

Examination of the throat showed only chronic laryngitis. Medical examination revealed negative findings in the lungs, but enlargement of the heart to the left, dyspnea and orthopnea. The blood pressure was 165 systolic and 85 diastolic. A diastolic blow of the aortic area was present. Repeated blood tests gave an anti-complementary reaction, and the reaction to a Kahn precipitin test was reported as from 1.5 to 2.

DISCUSSION

Dr. Howard Fox: I think that the chances are greatly in favor of lupus vulgaris. The eruption is symmetrical; the tip of the nose is eroded, giving it a beaklike appearance, and there are nodules on the upper lip which appear to be those of lupus. A late syphilid of the nose would rarely show such a symmetrical involvement.

Dr. Paul Gross: I would be inclined to consider this a case of lupus miliaris. The only diagnostic difficulties are the repeated anticomplementary Wassermann reactions, which delayed therapeutic trial.

Dr. Boleslaw Lapowski: What is the duration of the eruption?

Dr. Paul Gross: The duration of the eruption is two and a half years, which is rather long for syphilis.

Lymphatic Leukemia (Prurigo Lymphatica). Presented by Dr. J. Gardner Hopkins for Dr. Machacek.

M. M., a man, aged 60, married, born in Hungary, was seen in the dermatologic department of the Vanderbilt Clinic one year prior to presentation. At that time on the extensor surfaces of the arms and legs and scattered over the trunk and forehead were numerous infiltrated, dusky, papular lesions, varying in size from that of a pinhead to that of a bean, many showing follicular arrangement. Many of the lesions showed a scaly and also a crusted surface. The patient complained of intense itching. On the right buttock was a large, dark, almost black, sharply marginated lesion, the dark portion of which had the appearance of necrotic skin. There were many papular, necrotic lesions on the thighs. There was a superficial crusting of the genitals, and healed pigmented lesions were present on the lower extremities. There was a definite splenic enlargement, and the liver was also enlarged. There was a generalized adenopathy, and the left side of the neck was swollen.

A differential count of the blood showed: white cells, 30,600; polymorphonuclears, 13 per cent; lymphocytes, 72 per cent, and eosinophils, 3 per cent. The patient was again seen on September 16 and 28. On September 30, a blood count showed 89,000 white cells, with 80 per cent lymphocytes. The cutaneous condition had changed somewhat. There were large, erythematous, edematous areas

on the dorsum of the left hand and forearms, some with tiny vesicles in the center and others with large bullae. Similar lesions had occurred in the past, always accompanied by itching, which did not disappear until the bullae burst and drained.

Examination for tinea infection of the groin gave negative results. The patient had been seen by the medical department on Feb. 26, 1931, and at that time he complained of large lumps in the neck and under the arms. He had a generalized lymphadenopathy, enlargement of the spleen and liver and a cystlike formation on the left vocal cord, and he gave a history of penile sore and gonococcus infection two years previously. The Wassermann reaction was negative, and urinalysis likewise gave negative results. The patient showed roentgenologic changes of the lungs and apical pleura, which were finally ascribed as being due to emphysema and chronic bronchitis. The blood count at that time showed: hemoglobin, 78 per cent; red cells, 4,100,000; white cells, 173,000, and lymphocytes, 84 per cent. On March 11, 1931, when regional roentgen therapy was instituted, the blood count showed: hemoglobin, 82 per cent; red cells, 4,000,000; white cells, 237,000, and lymphocytes, 87 per cent. On May 20, the first pruritic, papular, pustular lesions developed, which were discrete and scattered over the neck and chest. At that time the white blood cell count was 53,000, with 80 per cent lymphocytes. The lowest blood count was noted on July 29, when the white blood cells dropped to 23,000 and the lymphocytes to 77 per cent. The patient had received twenty-six exposures to the roentgen rays. To the time of presentation, he had had thirty-one regional exposures to the axillae, neck, spleen and inguinal regions. Seven of these were anterior, and seven were from the posterolateral aspects of the spleen.

Sections from this case showed a papillary superficial outgrowth with markedly acanthotic epithelium in some places. The epithelium showed, among other changes, an edema and an infiltration with eosinophils. Numerous eosinophils were noted in the corium. The corium showed the most remarkable changes; these changes were tuberculomatous; there were numerous giant cells, often surrounded by a small group of shrunken irregular cells suggesting epithelioid cells. A large number of small round cells having the characteristics of lymphocytes were present. These surrounded hair follicles and blood vessels and often showed mitotic figures. There was also a diffuse infiltration of these cells in those portions of the corium where the more striking conglomerate tubercles were not seen. Definite areas of necrosis were present which showed in the eosinophilic débris, with pyknotic, irregular, nuclear material. This picture struck one as being, in general, similar to that demonstrated in a case reported by George J. Busman and Arthur R. Woodburne of Pittsburgh (Lymphatic Leukemia, *J. A. M. A.* **95**:1253 [Oct. 25] 1930). The miliary tubercles were not as pronounced, however, in this instance as in the material they studied. On the other hand, the blood changes were more striking. The peculiar and inconstant morphologic reactions of the lymphoblastoma as brought out by H. T. Keim, Lawrence McCafferty and others was further substantiated by this striking case.

DISCUSSION

DR. MACHACEK: The slide showed a great many giant cells surrounded by what appeared to be epithelioid and lymphoid cells and areas of necrosis, much the same picture as in the case reported by Busman and Woodburne of Pittsburgh.

DR. EUGENE TRAUB: How recently was the biopsy performed? If it was done lately, from which one of the various types of lesions presented by the patient was the specimen taken? He shows a great assortment of lesions, but from their clinical appearance now, the report of the section as read would hardly fit any of them.

DR. MACHACEK: A biopsy was performed about three weeks ago on a specimen taken from one of the papulonecrotic lesions present at that time on the thighs.

DR. OSCAR LEVIN: I think it is best to regard this patient as suffering from lymphoblastoma. He is apparently affected with a condition causing trouble in

the lymphocytic organs. Although the clinical picture suggests lymphatic leukemia, the pathologic changes in the excised piece of skin suggest tuberculosis. I would, therefore, prefer to classify this in the general group of lymphoblastomas, and not regard it as a frank case of lymphatic leukemia.

DR. ISIDORE ROSEN: This patient presents three different types of lesions: (1) small, skin-colored, firm, hyperkeratotic lesions, which are characteristic of prurigo lymphatica; (2) bullous and erythematous lesions, which are probably due to the toxins liberated by the roentgen therapy, and (3) nodular infiltrations in the skin, which are undoubtedly leukemic infiltrations.

DR. PAUL GROSS: It is difficult to classify the type of leukemic eruption this patient presents. As Dr. Rosen pointed out, the patient has lesions that followed roentgen therapy and could be called leukemids. There are a few lesions of a more tumor-like appearance, yet they do not quite fit into the picture of leukemia cutis propria. The most interesting are the bullous and hemorrhagic lesions, which are unique and, if anything, are closer to the leukemic exanthems described by Artz.

DR. MACHACEK: The lesions on the buttocks seemed to indicate infarction. Lesions appeared after roentgen therapy had been instituted, as I tried to point out in the history, and were of toxic origin. The main thing is the peculiar histology, which, as I mentioned before, was described in October of last year by Busman and Woodburne of Pittsburgh. At the end of the history, I mentioned Keim's work and an article written by McCafferty dealing with the curious manifestations of these lymphoblastomas. The different lymphoblastomas seem more or less to fuse into one another; Hodgkin's disease develops leukemic symptoms, for example.

LICHEN PLANUS BULLOSUS. Presented by DR. PAUL GROSS.

C. R., a man, aged 40, born in Ireland, married, was first seen at the Vanderbilt Clinic on May 8, 1931. At that time the lower third of both legs had many erythematous and scaly, pea to half dollar sized lesions of six months' duration. The patient had many varicosities on both legs and complained of occasional itching. A diagnosis of eczema due to varicose veins was made. The patient was referred to the varicose veins clinic, where he received intravenous injections for varicosities. He was seen again in the dermatologic clinic on June 24. The lesions on the legs had persisted. He also had scaling and maceration between the toes. Examination for tinea in the lesions between the toes gave negative results. The patient applied one-half strength Whitfield's ointment for two weeks without change in the condition, which meanwhile became severely pruritic. He was given fractional doses of unfiltered roentgen rays for three weeks. During that time the local condition became worse constantly. The patient was seen again on August 20, when he presented large bullous lesions on both legs which, after healing, left superficial scars. On the dorsa of both hands were many lesions varying in size from that of a pea to that of a dime; some of them were papules; others were distinctly of the iris type. Pruritus was very severe and was worse following roentgen therapy. The patient had been applying calamine lotion with 0.5 per cent phenol to the involved parts. On September 2, there were many new lesions on the wrists and thighs. These lesions presented all the characteristics of lichen planus, and were pinhead sized or slightly larger, violaceous, polygonal and shiny. New bullous lesions were still appearing on the legs. The lesion on the left wrist was excised for biopsy.

Two cubic centimeters of mercuric salicylarsenate was injected intramuscularly; as the patient was unable to come regularly for the injections, he was given solution of potassium arsenite by mouth, the dose being increased from 1 drop to 10 drops twice a day.

On September 15, the condition was practically unchanged. New lesions had appeared on the arms and the legs, but the pruritus was less marked. On September 25, the lesions on the dorsa of the hands and on the arms were much

paler and flatter. New bullae were still appearing on the legs. Roentgen therapy was again ordered, and two days later there was a recurrence of severe pruritus over both legs.

Section of a piece of skin removed from the right wrist showed a definite keratosis of the epithelium in some places. Certain portions of the granular layer also showed a heaping up of cells. There was edema of the epithelial layers. The basal layer was frayed. Very little pigment was seen in the basal cell layer. There was a marked infiltration of the corium. The cells were for the most part lymphocytes, although larger mononuclear cells were distinguished. The infiltration of the cells was for the most part confined to the superficial corium and the vicinity of the blood vessels. The histologic diagnosis was lichen planus.

DISCUSSION

DR. LOUIS TULIPAN: Lichen planus lesions are present in this case. We have to take it for granted that the patient had bullae. We had a patient with a case similar to this recently in our clinic who had been treated for lichen planus for quite a long time. He had received mercuric salicylarsenate and roentgen therapy, and then bullae developed. I would accept the diagnosis.

DR. FRANK C. COMBES: Did the bullae appear on the lichen planus lesions or did they appear independent of the lesions?

DR. PAUL GROSS: The patient came to the clinic some time ago and has had a number of treatments, but there were, as could be seen by the photographs in the beginning, distinct bullous lesions, and the blisters formed on top of the lichen planus efflorescences.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN?). Presented by DR. LEWIS BYRNE ROBINSON.

C. Mc., a woman, aged 53, married, was first seen on Sept. 28, 1931. About five or six weeks prior to presentation, she had noticed a few "pimples" on the left arm and thigh which were itchy. Two weeks prior to presentation, her present skin condition developed, which had spread rapidly thereafter. She had been taking "alophen" pills. There were two other medications the nature of which could not be ascertained at the first presentation.

On examination, an eruption was found which consisted of numerous papular, erythematous lesions and flatter patches of pityriasis rosea-like scaling, with a circinate appearance. The eruption appeared to be a toxic erythema probably caused by a drug, but an interesting feature of the case was that in spite of the symmetrical involvement of the buttocks and thighs, of the upper extremities only the left arm showed an eruption, while the right arm was completely free. This fact could be explained by the trophic and circulatory changes of this extremity due to a previous mastectomy.

DISCUSSION

DR. FRED WISE: The eruption does not appear to me to possess the characteristics of a drug eruption, I think it more likely that it was caused by some external irritant, such as a woven abdominal girdle.

DR. PAUL GROSS: Alophen contains aloe besides phenolphthalein, which may be the cause of a drug eruption. The important feature of this case should be mentioned before further discussion. The patient had a generalized eruption decidedly suggesting a toxic condition, but while the lesions were symmetrical on the buttocks and thighs, only one arm was involved. The explanation was given the presence of a scar that followed a radical operation on the breast. In other words, on the side of the operative scar, the trophic and circulatory conditions were changed, so that the toxic agent did not produce skin eruption.

DR. HOWARD FOX: I agree with Dr. Gross that the appearance of the eruption is that of one produced by an internal rather than an external cause. As the patient has taken several kinds of medicines, it seems that the burden of

proof is on the presenter to show that the eruption is due to some specific drug. If a similar outbreak should follow a subsequent administration of one of these drugs, we could reasonably suppose that it was caused by this drug. The lesions do not have the appearance of a phenolphthalein eruption as there are no well defined erythematous plaques or pigmentation.

PRURIGO NODULARIS. Presented by DR. HERMAN GOODMAN.

L. R., a boy, aged 17, single, began at the age of 6, following a cut on the ankle, to have a boil with pus, located just above the internal malleolus of the left ankle. The boil itched, and he scratched it. Almost immediately, two more boils developed above the site of the first lesion. These also itched and were pustular. Eight of the lesions had developed by the time he was 7 years old. They continued to itch, and were of the same size as at the time of presentation. The patient did not remember when the lesions on the foot first appeared, but he stated that the one in the popliteal space had begun three years prior to presentation. He had not been ill from it at any time. A lesion was excised at the Brooklyn Hospital in September, 1928.

The patient's previous health had been good, except for pneumonia at 16 years. He stated that he used cathartics occasionally, but no medicines to make him sleep and no blood tonics. The family history was irrelevant.

On Aug. 1, 1931, the Wassermann reaction was negative. A trichophytin test and a smear and culture for sporothrix also gave negative results. Biopsy showed an epidermis that was hyperkeratotic and covered by a moderate corneum. The blood vessels were dilated and thrombosed. The endothelial cells of the blood vessels were dilated and surrounded by connective tissue.

DISCUSSION

DR. HOWARD FOX: All the cases of prurigo nodularis I have seen have been in women; the eruption is symmetrical and intensely itchy. I could see no evidence of itching in this case. I would certainly exclude the possibility of prurigo nodularis.

DR. OSCAR LEVIN: This case is of interest because a differential diagnosis from sporotrichosis and tuberculosis is necessary. The skin presents a unilateral, linear, hyperkeratotic lesion with several discrete nodules. The nodules are scaly, elevated, verrucose and slightly inflamed. At first sporotrichosis and tuberculosis were suggested, but were easily excluded. There are no signs characteristic of prurigo nodularis. The diagnosis suggested is that of nevus unius lateralis.

DR. PAUL GROSS: I think that the two diagnoses mentioned, nevus unius lateralis and prurigo nodularis, would be compatible in this case. On the one hand, the linear nevus is frequently itchy and may give rise to a secondary neurodermite. On the other hand, the prurigo nodularis has been considered by many authors a peculiar type of circumscribed lichenification.

DR. GEORGE C. ANDREWS: I think that it is a case of nevus unius lateralis on account of the distribution and long duration. Microscopic examination need not show nevus cells with such a diagnosis. One would not expect them.

DR. LOUIS CHARGIN: Prurigo nodularis is a bilateral eruption, occurring mostly in females and not in young persons; it is always symmetrical and always chronic. This picture certainly does not fit that presented by the patient. Nevus unius lateralis can become eczematized and simulate prurigo nodularis.

If we accept prurigo nodularis as a clinical entity, then the case before us is not one of that disease. Prurigo nodularis is, as a rule, bilateral, occurs mostly in females and not as a rule in young people, is almost always symmetrical and appears mostly on the lower extremities. This description does not fit in with the case presented. My impression is that we are dealing with a nevus that has become eczematous, and all we can say is that some of the lesions resemble those in prurigo nodularis.

DR. CHARLES WOLF: The clinical diagnosis of prurigo nodularis is the most likely, because the patient gives a history of intense itching following the appearance of the lesions, and there is a distinct separation of the lesions.

DR. FRED WISE: I agree without hesitation with the diagnosis of unilateral linear nevus, despite the fact that the individual lesions closely resemble those of prurigo nodularis.

DR. HERMAN GOODMAN: The boy has a unilateral type of lesion running in a line and made up of six or seven individual lesions. The lesions did not appear at one time. When he was 5 or 6 years old, one lesion appeared, and then others followed with the years. The most recent is of two years' duration and is in the popliteal space. If we take one lesion alone, say the most recent one in the popliteal space, and analyze it, we note that it is a solid, elevated nodule covered by thickened keratin. There is nothing in that lesion that suggests a nevus. The surface is furrowed and gives the impression of scratch marks, which the patient readily admits, since he complains that the lesions itch. Nevi do not give this symptom. I believe that it is the order of the half dozen lesions in the semblance of a line that makes it so easy to suggest linear nevus, yet the lesions are not directly in line. If one draws a line through the lesions, from the uppermost one in the popliteal space to the one closest to the toes on the edge of the foot, one would draw a curve. Further, the lesions on the lower leg do not appear to be the same as the keratotic lesions along the sole.

There is agreement in the textbooks that we do not know what prurigo nodularis is. It is true that most cases show lesions on both legs. Can this be used as the only argument against admitting this case into the group of prurigo nodularis? It is unusual to have unilateral prurigo nodularis, but is it impossible? In this case, the individual lesions fit the description of the lesions of prurigo nodularis. The itching is severe, as it is in that disease. The lesions are discontinuous in site and in time of appearance. This is not the story of nevus unius lateralis. We will study the patient further with a view of making the diagnosis prurigo nodularis unius lateralis.

A CASE FOR DIAGNOSIS (LICHEN SCROFULOSORUM?). Presented by DR. FRED WISE.

L. R., a girl, aged 2 years, applied for treatment for a rash on the forearms, cheeks and thighs of about four weeks' duration. On the upper quadrant of the left buttock was an area approximately 3 inches in diameter, which presented a group of yellowish-brown, agminate, flat-topped, shiny papules, varying in size from that of a pinhead to that of a millet seed, seated on a circumscribed area of infiltrated tissue. This area had been present since birth and appeared to be a lichenoid papular nevus. There was also a small pigmented nevus on the outer upper portion of the left arm.

The lesions for which the child was being presented appeared on the upper extremities about four weeks prior to presentation. They consisted of grouped, pinhead-sized, lichenoid, pinkish lesions, many of which were arranged around a somewhat centrally depressed, lighter colored midarea of skin which had undergone partial involution; in other words, like lichen scrofulosorum. Such formations were seen chiefly on the forearms. Other areas presented groups of isolated, flat, shiny, pinhead to millet seed sized papules, resembling both lichen planus and lichen nitidus.

Physical examination gave negative results, and subjective symptoms were entirely absent.

Tuberculin tests were performed on the day of presentation, and the results were to be reported at a subsequent meeting. Roentgenograms of the lungs were to be taken at the time of the next visit to the clinic.

The active papular lesions were confined to the upper extremities; a few were also seen on the cheeks, with some scattered areas on the legs, thighs and feet.

SUBSEQUENT NOTE.—Histologic examination was suggestive of eczema. All tests for tuberculosis gave negative results. The lesions cleared up in a few days after the use of 3 per cent resorcinol paste.

DISCUSSION

DR. EDWARD MALONEY: I should say that clinically this is a case of lichen scrofulosorum.

DR. FRANK C. COMBES, JR.: I agree with the diagnosis. An unusual feature in this case is that the lesions are more or less confined to the extremities. In lichen scrofulosorum there is a tendency for the lesions to group on the trunk.

DR. HOWARD FOX: Did this child have any general evidence of tuberculosis? The question is asked, as this type of tuberculid is invariably associated with active tuberculosis, which is not the case in some other tuberculids, such as the papulonecrotic type.

DR. WALTER J. HIGHMAN: I do not think, on the clinical grounds of ordinary everyday diagnosis, that there can be any doubt that this is a case of lichen scrofulosorum. I think that the lesions may be very evanescent in this patient. The type of tuberculid described in Vienna twenty years ago and in this country by Jerome Leopold is that of a type of tuberculid representing a bacteremia in the literal sense, from a cryptic focus of tuberculosis usually terminating in meningitis.

FOX-FORDYCE DISEASE: CHRONIC LYMPHADENITIS. Presented by DR. B. KESTEN.

M. A., a colored woman, aged 34, was first seen at the Vanderbilt Clinic on Feb. 18, 1931, when she sought relief for itching "pimples" in the axillae, over the mammary glands, on the pubis and on the labia majora of five months' duration. The patient had first noticed the rash in the axillae a few days after shaving. She scratched these areas, and "pimples" and also a succession of abscesses (about nine) began to appear, which required incision. This condition persisted, and about two months later pruritus started over the pubis and vulva and then papules began to appear. Recently, the patient had noted papules on the mammary glands. These itched occasionally. The itching was so intense that the patient was unable to sleep or work and had lost about 10 pounds (4.5 Kg.).

The patient's menses had begun at about the age of 13, occurred regularly about every twenty-eight days and lasted four days without dysmenorrhea. During the past year, the menses had occurred about every twenty-four days and the flow had been intermittent. There was no dysmenorrhea. There had been no complete pregnancies. Pararectal abscess and fistula in ano had occurred about ten years previously. One brother had died of tuberculosis.

Examination of the skin showed the hair to be scant in both axillae, and there were about a hundred papules. They were most prevalent at the borders of the hair regions, particularly anteroposteriorly. From ten to fifteen papules were distributed over the areola of each mammary gland. The entire hair region of the pubis and labia majora was covered with them. These papules were from 2 to 5 cm. in diameter; they were firm, rounded, smooth and discrete, the color of the surrounding skin, and occasionally they were surmounted by a small white scale.

General examination revealed pyorrhea; the lungs showed a dulness at both apexes. There were generalized adenopathy (discrete, firm and tender), symmetrical leukodermal patches on the labia and induration in the left labia majora; the cervix was slightly eroded, and the uterus was normal.

The Wasserman and Kahn reactions of the blood were negative. The urine was normal. A blood count was normal. The basal metabolic rate was minus 3 per cent. A roentgenogram of the chest showed it to be normal, with the

exception of tiny deposits of calcium, indicating an old and healed tuberculous process; roentgen examination of the abdomen showed no evidence of mesenteric nodes.

For three and a half months the papules in the axillae were desiccated, and a papule was excised for study at weekly or biweekly intervals. The latter was done in an attempt to study any cyclic changes in the apocrine glands which might be correlated with the menstrual cycle. For the following four months the patient received occasional roentgen treatments to all areas. There had been no new lesions during that time; many of the old papules disappeared, and the itching decreased markedly. During the first three months of observation the axillary abscesses required excision and drainage. At the end of that time, a course of staphylococcus toxin was begun, and for the last three months the patient had remained free from abscesses.

Specimens of the papules excised from the axilla for biopsy over a period of three months had been studied by Dr. Machacek, and showed the following:

There were varying degrees of both polymorphonuclear and lymphocytic infiltration about the apocrine glands, which showed direct involvement by an inflammatory process and in some cases were obliterated by fibrosis. A few large vacuolated epithelial cells remained. The inflammatory process extended along the duct and involved particularly the outlet in the follicular funnel; the hair follicle was also involved, so much so that in several instances there was a definite cystic degeneration of both the follicle and the apocrine duct junction. The pilometer muscle also was infiltrated with polymorphonuclears and lymphocytes. A diffuse edema and an infiltration of the corium were noted. Spongiosus, acanthosis and keratosis were noted in the superficial epithelium. These changes were particularly marked one, two and five days after menstruation. A proved absolute relation to menstruation was not maintained.

NEUROTIC EXCORIATIONS. Presented by DR. PAUL GROSS.

E. A. B., a Negro, aged 54, single, was first seen at the Vanderbilt Clinic on Aug. 31, 1931. He gave a history of having had an eruption on the hands for eight months; previous to that time he had had similar eruptions on the body for several years.

On examination the patient showed a number of palm-sized and larger, darkly pigmented areas which were covered with pea-sized vesicles filled with clear fluid. Some of the vesicles were scraped off and showed a bleeding corium. In other places the lesions were healing. There was only a slight infiltration in some of the pigmented areas.

Neurologic examination revealed the absence of abdominal, pharyngeal and cremasteric reflexes and sluggish plantar reflexes. There was no neurologic evidence in favor of pellagra.

On September 4 the patient was admitted to the hospital, and a general medical examination revealed no pathologic findings except mucous colitis. Examination of the blood showed: hemoglobin, 58 per cent; red cells, 4,500,000, and white cells, 8,200, with 74 per cent polymorphonuclears and 26 per cent lymphocytes. The blood pressure was low, 102 systolic and 74 diastolic. The previous history showed that the patient had had malaria as a child and tropical fever while in South America. Psychically, the patient showed a distinct neurasthenic and hypochondriac tendencies, continuously worrying about his health, his intestinal function and his diet. He had been a food faddist for several years, excluding vegetables entirely from his diet.

When examined on September 4, the patient's skin condition had changed completely; except for a few pustules, the skin eruption consisted only of depigmentation, depigmented scars and large areas of hyperpigmentation. A few crusted excoriations were still present, especially on the ankles. The distribution was rather symmetrical on the neck and over the shoulder blades. The midscapular region was entirely free, and the lower dorsal region again showed involvement.

The backs of the hands, the elbows, the buttocks, the inner aspect of the thighs and the inner and outer aspects of the ankles were also affected. It was obvious that the outer surface of the left ankle showed a much smaller area of involvement than that of the right ankle.

The Wassermann reaction of the blood was negative, and a lumbar puncture likewise gave negative results.

A diagnosis of extensive neurotic excoriations was made. The rapid recovery, as well as the confession of the patient and his whole neurologic make-up, seemed to favor such a diagnosis.

NEW ENGLAND DERMATOLOGICAL SOCIETY

WILLIAM P. BOARDMAN, M.D., *Secretary*

Regular Meeting, Oct. 14, 1931

ARTHUR M. GREENWOOD, M.D., *in the Chair*

DERMATITIS HERPETIFORMIS? Presented by DR. BERNARD APPEL.

CASE 1.—B. B., a white boy, aged 5, an American, had had an eruption on the extremities and face every spring and summer since birth. The lesions developed on the sites of trauma, starting as papules which quickly became crusted and infected, occurring in groups of three and four, mostly over the ankles, the backs of the hands and the face; they lasted for several months and left small scars, never any vesicles. The lesions had grown progressively worse during the past two summers. Over the face and extremities were numerous small varicelliform scars and a few scattered discrete papules, an occasional one crusted over.

Treatment with ammoniated mercury gave good results in the impetiginous lesions; there was also treatment with a lotion containing zinc oxide and phenol.

CASE 2.—E. A., a school girl, aged 14, an American, had had an eruption on the extremities for the past eight years, principally in the spring and summer, beginning as groups of from two to four papules, with intense itching at the start, which later subsided when scratched. The lesions lasted about a week and healed slowly, leaving bluish-red scars. The eruption was worse over the lower part of the legs and forearms. On the extremities were many small scars in various stages, bright red and varying from bluish to white. There was a group of excoriated papules on the inner part of the right thigh, one on the right leg and one on the ankle and an occasional papule on the left leg. The lesions were discrete.

The patient was treated with potassium arsenite, which was poorly borne and then omitted. Considerable relief was obtained with calamine lotion.

CASE 3.—A. V., a white boy, aged 3, an American, had suffered from an itching eruption, generalized particularly over the extremities and neck, which had recurred every spring and summer since birth. The lesions had started as papules, but they often appeared as small, deep-seated vesicles. Itching was worse at the onset of the lesions. Fine pigmented scars resulted. At presentation, he showed a papular eruption, chiefly grouped over the ankles, knees, wrists, elbows, neck and buttocks. There were some lesions in the intervening areas; all lesions were discrete and left purplish-red, flat, soft scars similar to those in varicella. A few weeks before presentation, there were deep-seated vesicles over the ankles.

The patient was treated with potassium arsenite and calamine, with little effect. A dilute solution of iron chloride gave the best results at the onset of the attack.

DISCUSSION

DR. L. J. CUMMINS: In case 2, with the lesions and scars on the arms and legs, I could not help feeling that there was a large element of factitia.

DR. W. P. BOARDMAN: In case 3, I was interested in the fact that the condition is worse in summer when exposed to the sun, which is certainly unusual, for dermatitis herpetiformis is usually improved by the use of the sun lamp.

DR. J. H. SWARTZ: In case 3, the mother said that the lesions usually began as white blisters, but on further questioning I decided they were really wheals, as I produced a wheal by rubbing. I wondered if the condition was not a papular urticaria. I think the eruption in case 2 is also papular urticaria.

DR. A. M. GREENWOOD: It seems to me that all three cases come under the classification of papular urticaria, with the possibility of the second one being factitial or with elements of factitia in it.

DR. F. P. MCCARTHY: This is the type of case that, in the summer, one would frequently pass over as being the result of insect bites, but the fact that the condition continues well into the fall eliminates that diagnosis.

LUPUS VULGARIS? Presented by DR. E. L. OLIVER.

M. C., a man, aged 24, an Italian, a maker of ice cream, was admitted to the skin department of the Massachusetts General Hospital on account of an eruption of eleven months' duration. One year before presentation, while training as a pugilist, the patient received many blows on the nose. One month later he first noticed a red, shiny swelling of the right ala nasi; there was no pain or local heat. Eight months prior to presentation a small pustular eruption developed over the affected area, which by that time included the whole right side of the nose. He received treatment with the Kromayer lamp in the New York Skin and Cancer Hospital for two months. Meanwhile, the lesion became raw; then it was covered with dry, scaly skin, and spread to the left side of the nose, the right side of the upper lip and the right side of the chin. During the preceding two months, the lesion on the chin had healed, but the nasal lesion had spread bilaterally. The entire nose was covered with thin, red skin which was overlaid with small bits of scaly, dry skin. On the right side, especially about the ala nasi, a great part of which was missing, there were bits of a yellowish, crusted exudate. A patch of the same sort of skin about 1 to 1.5 cm. wide extended from the right nostril down over the upper lip to the mouth. The left side did not appear to be as extensively affected as the right, and the lesion did not extend much above the bony part of the nose. The tissue underlying the affected area was very soft and delicate, more so than normal. When the skin of the nose was blanched with a microscope slide, a brownish "baked apple" color resulted. A nasal discharge was attributed to a cold.

No report was obtained on a biopsy.

DISCUSSION

DR. J. G. DOWNING: I think this would be a good case in which to try electrocoagulation. Have you used endothermy or electrocoagulation in these cases?

DR. E. L. OLIVER: I have not used electrocoagulation. It has been used in New York with good results. I think excellent results are obtained with curetting, and one can tell how far the process goes. With endothermy a good deal of healthy tissue may be destroyed. The destruction resulting from operative measures is great. In the case of a girl very little of the nose was left after the operation, and the parents were shocked. Although the result from our point of view was very good, the parents thought we had gone too far. The case was one of hypertrophic lupus. The tissue was spongy, and curettage went deep.

LUPUS PERNIO. Presented by DR. WILLIAM J. MACDONALD.

I. G., a white woman, aged 22, an American, a bookkeeper, had had an eruption on the dorsal surfaces of the fingers since February, 1931, supposedly following a manicure. The surface of the body elsewhere revealed no evidence of

similar lesions. The general health was good, and the alimentary system and the heart were normal; the menstrual history included dysmenorrhea. The teeth were good. There was no history of the use of drugs, or of a previous eruption. The patient had never been in contact with any external irritant. The extremities were cold; the patient stated that she suffered from chilblains. The dorsal surfaces of several fingers of both hands showed discrete, infiltrated, raised, violaceous red, dime-sized, painless lesions, with evidence of atrophy in several places. Several finger-nails showed slightly dystrophic changes, with irregularly eroded free borders. The Wassermann reaction was negative. The urine showed a specific gravity of 1.015, acid, a trace of albumin and no sugar, bile, pus or blood.

The patient had had no treatment.

DISCUSSION

DR. E. L. OLIVER: I think the circulation plays a great part in this case. If we could increase the circulation by any means, such as cutting the nerves, we might be able to clear up the disorder, as in Raynaud's disease. I think the so-called lupus pernio occurs usually in young people. It is not likely to occur in persons with thoroughly good circulation.

DR. W. J. MACDONALD: Is it usual to find these atrophic jagged edges in lupus pernio?

DR. J. G. DOWNING: Were roentgenograms taken of the distal phalanges? Last year at Copenhagen some slides and a roentgenogram of changes in the distal phalanges were shown which were very interesting.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. RUDOLPH JACOBY.

A. B., a white woman, aged 58, an American, a housewife, had an eruption on the face, neck and extensor surfaces of the arms which started in May, 1931. The patient had two living children and another had been stillborn. Three years before presentation, an appendectomy, ventral suspension, perineal repair and removal of hemorrhoids were done at the same time, with slow recovery. During the winter of 1931, she complained of some palpitation and shortness of breath and had an occasional trace of bloody sputum. The blood pressure was normal. Roentgenograms of the heart and lungs were negative. There had been a slight loss of weight. There was no history of the use of drugs. She had been frying large quantities of doughnuts twice weekly, because her husband had been out of work. In May, an intensely itching, erythematous eruption had appeared on the face and the neck, which soon spread to the arms. The lesions varied in size and shape, but most of them were round with infiltrated margins. Many of the lesions had fused, forming areas 2 or 3 inches (5 or 7.6 cm.) in diameter. The lesions on the arms were on the extensor surfaces and were violaceous. The hair was falling out, and there was a slightly edematous appearance to the face.

Results of the examination of the blood showed: hemoglobin, 70 per cent; red corpuscles, 4,140,000; color index, 0.84; white corpuscles, 3,200; neutrophils, 56; lymphocytes, 38, and no eosinophils. There was slight anemia with leukopenia. The platelets were slightly diminished. The renal function was normal; urinalysis was negative, and allergy tests gave negative results.

The patient was treated with ultraviolet rays; local and systemic treatment was given by her local doctor, without improvement.

•

DIFFUSE LUPUS ERYTHEMATOSUS? Presented by DR. J. H. SWARTZ.

A Finnish woman, aged 34, a hair-dresser, was admitted to the ward for cutaneous diseases of the Massachusetts General Hospital. The present eruption began about the last of April, 1931, as a small red papule just below the right eye, and spread gradually until it involved the entire face, except the upper part of the forehead and the area around the mouth. On August 12, the patient had four teeth removed, and the next day the lesions spread over the ears, and

scattered ones appeared on the neck and the forearms. A v-shaped red area also appeared on the front of the neck and the chest. At the time of presentation the face showed a bright red eruption, smooth, with an irregular border, without scales. On and back of the ears there was a similar redness with slight scaling. On the front of the neck there was a blotchy area similar to that on the face. The dorsal surfaces of the hands and forearms showed a discrete, red, macular eruption. The lateral and posterior aspects of the upper part of the arms and the lower part of the legs showed many minute red papules.

The Hinton reaction was negative. The urine was negative. Several examinations of the blood showed: hemoglobin, from 65 to 70 per cent; red corpuscles, about 4,100,000, and white corpuscles, from 2,500 to 4,000; the differential count showed: neutrophils, from 70 to 85 per cent; lymphocytes, from 15 to 30 per cent, and eosinophils, from 1 to 2 per cent. There were marked anisocytosis and some poikilocytosis; the platelets were much reduced, and there was no obvious acromia. Later the platelets increased, and the red blood corpuscles were more regular.

The nonprotein nitrogen of the blood was 25 mg. per hundred cubic centimeters; the chlorides, 633 mg., and the blood sugar, 89 mg.

Culture of a catheterized specimen showed B. coli. A blood culture showed no growth.

A roentgenogram of the chest showed dense mottled dulness involving the apex and first interspace of the right lung. The band of dulness had the density of calcium. There was a large area of mottling below the first rib. The left lung was clear; the diaphragm was normal, and the results of the examination of the gastro-intestinal tract were negative. There was an unerupted tooth in the area of the upper left third molar. There was no definite apical abscess. There were carious lower teeth, with periapical infection.

The patient was treated with mild local applications. A transfusion of 500 cc. of blood was made on October 5. The impacted molar and the infected teeth were excised under local anesthesia.

LUPUS ERYTHEMATOSUS. Presented by DR. MYER M. TOLMAN.

A man aged 26, an American, a general worker, was admitted to the Boston Dispensary Clinic for an eruption on the face of nine years' duration. He showed typical lupus erythematosus with butterfly arrangement on the face. From November, 1927, to July, 1930, the patient received 8,855 mg. of a gold compound. In December, 1930, he showed a slightly itching, scaly, seborrheic-like eruption on the upper part of the arms, chest and thighs, and treatment with the gold preparation was stopped. This eruption cleared up by the use of an ointment by Jan. 22, 1931. From February to April the patient received 80 mg. more of the gold compound and then icterus developed, with an enlarged liver and a palpable spleen. From June to October he received seventeen injections of bismuth. The eruption on the face, which had responded very poorly to the gold therapy, improved following the use of bismuth.

DISCUSSION ON THE CASES OF LUPUS ERYTHEMATOSUS

DR. L. J. CUMMINS: I was interested in Dr. Jacoby's and Dr. Swartz' cases. In the latter, I thought, the condition was an eruption due to phenolphthalein. The patient gave a history of having chronic constipation and of having taken a great deal of medicine. She told me that in the last three months she thought she had taken as much as 5 pounds of pills for the bowels which contained phenolphthalein. The first patient also gave a history of a sudden onset after severe sunburn and no previous illness, and the only thing she had taken was "some medicine," which proved to be agarol. These two cases look very similar to me.

DR. R. JACOBY: We admit that both of these patients have taken a lot of pills and that the appearances are similar, but three quarters of the people in the

world are taking phenolphthalein all the time. I think they are cases of lupus erythematosus disseminatus and would suggest as a matter of treatment plasmochin. I have seen several patients who, treated with this in conjunction with a gold compound, have made marked improvements, and in two cases it was used without gold therapy, not intravenously, but by mouth.

DR. J. L. GRUND: Has it not been shown that gold therapy is unfavorable in these disseminated cases of lupus? What about bismuth?

DR. J. H. SWARTZ: In my case the particularly interesting part is the relationship of the patient's condition to the leukopenia. When she came to the hospital the white blood count was about 2,000. I ordered a transfusion, and the white count rose to 4,000, and there was rapid improvement. I wonder whether we are really dealing with a bone marrow depreciation. We have had some experience at the Beth Israel Hospital with cases with a low white count and bone marrow depreciation in which transfusion has helped a great deal, but the only question is whether the blood cells can be increased by repeated transfusions. I do not think my patient has had any treatments with gold preparations.

DR. GUY LANE: In regard to the acute cases of disseminated lupus erythematosus, I have recently seen a case that interested me. One of the most acute types I have ever seen developed in a nurse, starting with a small area on the face and developing into an extremely large lesion extending over the face and shoulder, chest and arms. She had an opportunity to go to Philadelphia, and I suggested that she see Dr. Schamberg. I was interested to see that treatment there was quickly begun with very small doses of a gold compound. I think the first dose was less than 5 mg. She had a small reaction after the first few injections and afterward not any. The doses were greatly increased, and when she returned the redness had entirely disappeared, and she had simply a pigmented area on the face, which has gradually been fading. The last two or three injections given in Philadelphia were in a solution of sodium thiosulphate. She made marked improvement.

DR. E. L. OLIVER: I think one often sees brownish pigmentation in these cases, especially at the borders of the lesions after treatment with a gold compound.

GRANULOMA ANNULARE. Presented by DR. BERNARD APPEL.

O. P. D., a school girl, aged 15, an American, was admitted to the outpatient department of the Boston City Hospital. She showed an eruption of one year's duration, the onset of which was insidious, and which caused no subjective symptoms. Over the left elbow was a pink lesion about 1 cm. in diameter and horseshoe-shaped, one segment being flat and quite shiny. About 2 inches (5 cm.) away from the lesion, on the extensor surfaces of the forearm, was an annular lesion about 1 cm. in diameter, with a pinkish-red, shiny surface. A small satellite lesion was near this one, similar in appearance, about 4 mm. in diameter. Under treatment with salicylic acid, 10 grains (0.65 Gm.), oil of cade, 10 mm. and zinc oxide ointment, 1 ounce (29.57 cc.) there have been a definite softening and flattening of the lesion.

DISCUSSION

DR. A. M. GREENWOOD: I heard Dr. Towle suggest treating the patient with ethyl chloride. I think that these patients do so well with roentgen treatment that it hardly seems necessary to use a destructive agent.

DR. E. L. OLIVER: I have seen some of Dr. Towle's patients treated with ethyl chloride, and, as I remember, he obtained some pretty good results.

DR. W. P. BOARDMAN: In that connection, I showed a small child with granuloma annulare on the face and hands at the previous meeting. I treated her with very small doses of roentgen rays, and the condition cleared up, but about three or four months later she came back with lesions on the feet. I have just given her another course of roentgen treatments, beginning with three small

doses, and the lesions seem to be disappearing again. I wish to ask Dr. Greenwood about recurrence after roentgen treatment.

DR. A. M. GREENWOOD: I think that if the lesions are not completely cleared up, they do recur.

DR. E. L. OLIVER: Were the second lesions in situ, Dr. Boardman?

DR. W. P. BOARDMAN: Not exactly. I naturally treated a child about 4 years old cautiously. I suppose I did not give treatment enough. I wonder if with more treatment the lesions would stay away for good?

DR. E. M. STANDISH: What dosage did you give?

DR. W. P. BOARDMAN: I gave 15 per cent of an erythema dose, three doses a week apart. The second time I gave 10 per cent, and the lesions now seem to be disappearing rapidly.

TWISTED HAIRS (CONGENITAL ANOMALY OF DEVELOPMENT OF A GROUP OF FRAGILE HAIRS). Presented by DR. F. RONCHESE.

A. B., a white girl, aged 8, an American, was admitted to the outpatient department of the Rhode Island Hospital. Since birth she had had the present trouble with her scalp. The occiput of the scalp showed partial alopecia. The scalp hair was of a wild, bushy appearance. The individual hairs were frizzled, twisted and fragile, many of them broken off at various lengths. The Wassermann reaction was negative. Urinalysis, examination of the blood, differential count and chemical analyses were negative. The basal metabolism was plus 12. Examination and culture of the hairs gave negative results. The resistance to stretching and elasticity was below normal. Immersion in a caustic solution (10 per cent sodium sulphide) showed a swelling and bursting of the hair in a much shorter time than normal for hair of the same color and for a person of the same age as the patient. Sections of scalp showed various degrees of atrophy of the sebaceous glands, plugging of the opening of the follicles by layers of keratotic tissue and twisting of the hair within the follicle. Cross-sections of the hairs showed an oval shape.

The patient was improving under treatment with wool fat cream. She is now using a cream containing cholesterol and salicylic acid, which gave very good results in one of the cases recorded in the literature.

DISCUSSION

DR. JOHN LANE: Has a case like this been described before? I am entirely unfamiliar with this condition. It looks like spindle hair. Clinically, the back of the head looks like the woolly nevus described by Dr. Wise a few years ago. This is entirely new to me. Did you find anything on the condition in the literature?

DR. F. RONCHESE: I found one case only.

LICHEN PLANUS ATROPHICUS. Presented by DR. J. H. SWARTZ.

R. F., a woman, aged 23, a Lithuanian Jewess, unemployed, came to the Skin Clinic of the Massachusetts General Hospital with the history of white spots on her back occurring at varying intervals. They began one year before the presentation of this case. The present lesions had been appearing since the middle of the summer. For two weeks prior to presentation there was itching on the back and chest. Examination showed areas of depigmentation, varying in size, with lichenified shiny papules at the borders on the right shoulder. There was a lichenoid lesion on the flexor surface of the right forearm. There were also a few similar lesions on the flank and on the anterior part of the chest. A biopsy is to be done. She has had no treatment as yet.

DISCUSSION

DR. J. H. SWARTZ: In addition to the pigmentation, I saw some definite atrophy and also some little groups of wheals and papules, and on examination of the forearm, I noticed a typical lichen lesion and one annular lesion beside it, which made me feel that the case was in the class of lichen planus atrophicans.

DR. J. W. LANE: I do not know what the condition is. One sees white spots like that sometimes following small lesions of psoriasis. It is rather hard to tell how much different the spots are from the normal color of the skin, because the patient was very much tanned from the sun during the summer. The condition may possibly be nothing but a leukoderma. I could not see any signs of atrophy. I did not see the lesions on the forearm; those I saw were on the back, and they were not atrophic.

DR. E. L. OLIVER: I saw the patient when she first came to the hospital; I examined her thoroughly, and I was satisfied that the condition was lichen planus. There were typical lesions, with papules around the border, like the spokes of a wheel. They were small, but definite, I think.

LUPUS VULGARIS. Presented by DR. J. H. SWARTZ.

A. H., a woman, aged 42, married, entered the skin department of the Beth Israel Hospital for a soft cauliflower-like growth on the nose with scattered verrucous nodules of a dirty yellow color. She had been treated in the past mostly with ultraviolet radiation and had responded somewhat to this treatment. The duration was over three years. The serologic examinations for syphilis were repeatedly negative.

Biopsy on Oct. 7, 1931, showed chronic inflammation. A diagnosis of lupus vulgaris was made, and the treatment outlined consisted of curetting.

DISCUSSION

DR. A. M. GREENWOOD: This is a case of hypertrophic tuberculosis of the nose.

DR. E. L. OLIVER: There did not seem to me to be much doubt about the condition being hypertrophic tuberculosis.

DR. W. D. WHEELER, Boston (by invitation): The first time I saw the patient was in 1929. She had been treated for eight years. An interesting fact in connection with her condition was that her husband had been treated for syphilis. Studies of her spinal fluid and repeated blood tests were made, which were always negative. Biopsy at that time showed lupus vulgaris. I treated her for lupus vulgaris for three months with electric desiccation, and the condition was getting worse. Two discrete lesions cleared up after two treatments of radium; we then began to use diathermy with the vacuum tube, three times a week, and the lesions cleared up completely in four months. Two months afterward there was a reaction, and the present erythematous condition followed; when elephantiasis developed two years ago, we took a roentgenogram and found an old tuberculous process on one side.

DR. J. H. SWARTZ: Have you any suggestion as to the connection between the elephantiasis and the lupus of the nose? Were there two distinct processes, or are we dealing with a tuberculous lymphangitis and a tuberculosis of the nose?

DR. G. A. WHEELER: The swelling decreases at times, but the condition is definitely elephantiasis.

DR. F. P. MCCARTHY: The elephantiasis is very suggestive of some disturbance of the lymphatics. Have you considered filariasis?

DR. J. H. SWARTZ: The examination of the blood for filariasis gave negative results.

DR. A. M. GREENWOOD: It is particularly interesting to see how many people under treatment for skin disease have edema of one side of the leg. I have never been able to explain the connection.

DR. J. W. LANE: If we saw a tuberculous process causing the destruction of the lymphatics, I think that would be pretty good evidence.

ROENTGEN DERMATITIS. Presented by DR. LORETTA J. CUMMINS.

B. K., a woman, aged 25, a stenographer, was admitted to the outpatient department of the Massachusetts General Hospital with an eruption on her chin of six years' duration. She had had about four hairs on her chin, and she went to an establishment which used the "Tricho" System, where she had eighteen weekly treatments. About one year after the last treatment the chin became very red. Then little red vessels and scar pits formed. The condition had grown worse in two years in that the chin was redder and the veins more prominent. The chin at presentation showed a shiny, smooth condition with beginning atrophy, telangiectasis and wrinkling.

DISCUSSION

DR. R. JACOBY: I have recently had a case of roentgen dermatitis that was caused by the Tricho System, in which I have been using electrolysis with a technic a little different than usual. This technic was suggested to me by Dr. MacKee of New York. One places the needles very close together, presses down just a couple of millimeters and uses a very low voltage current, that is, a couple of millimeters for not over a second, keeping the punctures very close together. In a great many areas this technic has been quite successful. In some areas on the girl's arm I have given rather severe burns with the Kromayer lamp, which have apparently cleared up some of the telangiectases. I approached this case with a great deal of doubt, but I felt that the patient should have something done for her, as she said she would go crazy if somebody did not do something for her.

DR. J. W. LANE: I suppose one is usually safe in giving treatment for these conditions, but I have absolutely refused to give these patients any sort of treatment, because ulcerations often occur two or three months after treatment. I think it is safer for us to let these patients alone.

DR. GUY LANE: Some years ago one of the older physicians in Boston told me about his attempt to treat with electrolysis a patient having telangiectasis in a chronic roentgen burn of the arm; he said that he got along all right for a while, and then in treating one telangiectatic lesion he produced an ulceration. It spread, and there was secondary infection, so that eventually there was a large area of ulceration which was very slow in healing. A little later I took the opportunity to treat a patient with an old roentgen burn with ultraviolet light and pressure; I reported that case. I treated the patient for a period of three years with ultraviolet light, using a small applicator, and I found at the outer border of the large lesions typical pigmentation, atrophy and telangiectases. The telangiectases cleared up fairly well, so that the element of redness was reduced when seen from a distance, but I also found that in treating areas inside the lesion, or areas of marked scarring, an ulceration was apt to be produced that took a long time to heal. In one such area in which comparatively small doses were administered there developed an ulceration that was very slow in healing. Again, I should hesitate about giving treatment with ultraviolet light and pressure over a large area, except possibly on the periphery. I think that there is also the possibility of later developments in which the risk would be too divided.

DR. J. H. BLAISDELL: This discussion recalls to me a young woman who came to the office a number of years ago who had been treated with roentgen rays for warts. I saw the patient with Dr. Burns. He made a statement that when a lesion is produced by roentgen rays a scar results; that the telangiectasis is, for all practical purposes, an effort on the part of nature to give added nourishment to the impaired part, and that if one removes it, one is certainly running the risk of breaking down the protection. This statement appealed to me as a logical conclusion.

DR. W. T. GARFIELD: About six or eight years ago, I showed a woman who a number of years previously had received roentgen treatments for tumor of the breast. She had at the time of presentation a large area of scarring and telangiectasis with ulceration. I treated her for the chronic ulceration with the sun lamp, and was very much surprised to find that the ulcers slowly healed and the telangiectasis markedly disappeared; the case was in the healing stage when I showed it. Subsequently, she consulted me because the ulcerated area had broken down again and she had a lump in the outer edge of the burned area. The tumor was taken out and diagnosed as carcinoma. The breast was removed and the glands of the axilla taken out, and the surgeon thought that he had removed all of the cancerous tissue. That was about three years ago, and I have not heard from her since.

DR. J. G. DOWNING: I recall one case in which my experience might be of practical use, especially in lesions on the extremities. I had a patient, a woman 38 years of age, who sixteen years before had been treated with roentgen rays for so-called eczema of the arm. She received a severe burn, which was excised and broke down. The main thing she wanted was to be relieved from the intense pain that kept her awake practically every night. She was getting sleep only in exhausted moments. I found, after having tried almost everything else that I could think of, that by massaging the entire arm and splinting it so that it was absolutely without motion, the pain was entirely alleviated, and the ulceration healed somewhat. The patient was recovering very well, when, unfortunately, a septic sore throat developed while she was on a two weeks' vacation, and she died in forty-eight hours.

DR. GUY LANE: I want to confirm what Dr. Blaisdell said about Dr. Burns' opinion by a reference to Dr. Holmes' idea as to the same thing. He has had a very large experience with sufferers from roentgen burns, and he feels that telangiectases are nature's means of assisting healing, and that interference with them to a very great extent means that one is running a risk of ulceration.

LUPUS ERYTHEMATOSUS. Presented by DR. HENRY BENJAMIN.

R. B., a school girl, aged 16, a Jewish-American, had an eruption that started nine months before presentation as a diffuse erythema over the entire face. It receded several days later to the cheeks and nose, and red papules appeared in this area. These enlarged and merged into one another, giving a mottled appearance. Two months later, circular lesions appeared on the arms. One appeared on the left knee one week before, and another on the upper part of the left arm three days before presentation.

Present examination showed erythema of the cheeks and nose, sharply outlined, containing numerous reddish, infiltrated, pinhead spots, covered by adherent scales. The follicles were enlarged. On the arms were circular and oval lesions about 1.5 cm. in diameter, fairly symmetrical on the extensor surfaces of the forearms and on the upper part of the arms. The lesions had red borders and slightly scaling centers. A similar lesion was present on the left knee.

The patient was treated with various ointments and washes. She received six ultraviolet light treatments three months from the onset of symptoms. The lesions grew slightly redder. For the two months prior to presentation she had been using Lassar's paste three times a day and liniment of soap, U. S. P., every second day. She had been exposed to the therapeutic rays. The lesions on the right arm had faded. The lesion on the face had receded at the border and faded somewhat until three weeks prior to presentation. Since then it had become redder.

DISCUSSION

DR. A. M. GREENWOOD: I should like to suggest the diagnosis of lupus vulgaris.

DR. W. P. BOARDMAN: The patient had some definite lesions that I thought corresponded to lupus nodules, but the character of the lesions on the arms and

the absence of any such nodules there made me think that the condition was more like erythema multiforme; however, one sometimes sees these toxic lesions also in lupus erythematosus disseminatus.

DR. A. W. CHEEVER: I thought the condition was probably lupus erythematosus, but there were lesions of the erythema multiforme type which were very interesting. Altogether, I thought the condition would probably come under that diagnosis.

SYPHILITIC BURSITIS. Presented by DR. J. H. SWARTZ.

Mrs. K., aged 56, a housewife, presented herself for treatment for a swelling of the right knee which had been present about a year and which had apparently followed trauma. Eight weeks before presentation, ulceration appeared on the lesion, and this ulcer had spread to the size of a dollar. The outlines were somewhat circinate. There was swelling over the patella and quadriceps tendon, and there was a slight fluctuation. The Wassermann reaction was positive. She has received no treatment.

DISCUSSION

DR. J. W. LANE: One does not see cases like this one often. A recent issue of the ARCHIVES had an article on that syphilitic condition (**24**:591 [Oct.] 1931). I had one patient some years ago with two such lesions, and I had them both excised. One was ulcerated like that in this patient, the other was not. The one that was not opened healed, but the other granulated. The patient presented is rather fat, and treating her would be more difficult. The cases are very striking.

DR. A. W. CHEEVER: These are striking cases, and I think that we ought to see more of them than have been presented at these meetings lately.

DR. J. W. LANE: The only place I know of where you can see such cases more frequently is the Bellevue Hospital. I do not remember more than thirty-five cases that have been reported, and the literature has been carefully searched for them. I have seen only one case besides this one.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. PERSKY, M.D., *Secretary*

Oct. 19, 1931

A. WALZER, M.D., *Presiding*

EPIDERMOLYSIS BULLOSA. Presented by DR. A. WALZER.

P. G., 4 years old, was the last of five children. The first and second had died at 5 days of age with bullous lesions. There was no history of a similar trouble in the family (the mother and father were third cousins). The father stated that he and his wife had had Wassermann tests made by the physicians of the board of health, and that the results were negative.

The patient had had these lesions since birth, and they had been reforming at different sites after the slightest trauma. They were present over the entire body and scalp. The primary eruption was a bulla. The lesions were of various shapes and sizes, some flaccid and others tense and some hemorrhagic. In some locations crusts and scales were present as the remains of the bullae. On the scalp, posteriorly, was one large patch, the skin over which was somewhat tight and atrophic, with portions of alopecia. On this patch was an elongated bulla, hemorrhagic and irregular. The fingers all showed bullae in various stages of develop-

ment, and some of the nails were missing. Nikolsky's sign was present. The child showed irregular areas of pigmentation. The mouth presented no lesions, and the teeth were not affected.

PRURIGO NODULARIS (?). Presented by DR. A. WALZER.

C. G., a woman, 46 years of age, married, had two children. She was always well. There was no history of ingestion of medicine. The condition presented was of two years' duration. It began with a terrific itching, especially over the extremities. The patient claimed that white elevated "spots" appeared at night and itched. When scratched they turned red, and by morning many of them had disappeared. Some persisted and eventually developed into the lesions exhibited.

At presentation the lesions were especially marked on the upper and lower extremities. The trunk and face were free from lesions. The eruption consisted of papules and nodules about the size of a pea. The color varied from that of normal skin to red. They were discrete, and some were flat while others were elevated, round and hard. None of them showed any crusting. Dermographism was present. The axillary and inguinal glands were palpable.

DISCUSSION

DR. J. SKEER: I think that the condition is prurigo nodularis, although the nodules are not the characteristic, large, cherry stone-sized lesions with pink or red skin that one sees in well developed cases. Probably it is because this case is not of long standing. There is no doubt that the condition is pruriginous, but I should like to have a biopsy report and also to rule out mycosis and leukemia.

PITYRIASIS RUBRA PILARIS. Presented by DR. L. J. FRANK.

D. C., a boy, 9 years old, was always well until nine months before presentation and eruption developed on the chest which soon covered the entire body. Mild itching was present. The lesions were distributed anteriorly over the entire trunk and face and to a lesser degree over the extremities. The primary lesion was a pinhead-sized erythematous papule with a glistening top. There were no lesions on the dorsal surfaces of the fingers.

DISCUSSION

DR. A. WALZER: I should not consider the condition pityriasis rubra pilaris, with regard to either its primary lesion or to its distribution. The primary lesion of pityriasis rubra pilaris is a follicular conical papule surmounted by a horny scale. These papules unite to form a large dry plaque. The backs of the fingers are usually affected. The patient does not show any of these lesions. I do not know in what classification to place the condition, but I do not think it is pityriasis rubra pilaris.

DR. M. J. CANTOR: This must be a very early case, because the lesions are not distinctly follicular. On the abdomen, the lesions are slightly red, but on the back and upper parts of the arms, some of the lesions look like those of the condition that has been called lichen albus.

DR. B. B. BERKOWITZ: My impression was that pityriasis rubra pilaris is very pruritic; yet this child shows no signs of pruritus. In fact, the history shows that there is only mild itching. I agree with Dr. Cantor that the lesions resemble those of so-called lichen albus.

A CASE FOR DIAGNOSIS. Presented by DR. E. A. GAUVAIN.

Mrs. E. N., a married woman, aged 24, had begun to have a general thinning of her hair at the age of 11 years. This was followed by premature graying. At the same time there was a change in the appearance of the finger-nails; this

condition at times improved on some fingers and became worse on others. Some of the nails had had an apparently complete recovery from previous involvement. At the time of presentation several nails were affected. The part of the nail immediately protruding from the nail fold was normal in appearance; the distal end was brittle, opaque and thinned and appeared to be pitted. There was no apparent involvement of the nail fold.

DISCUSSION

DR. M. J. CANTOR: On first appearance, the condition suggests either tinea or psoriasis. The patient does not have psoriasis elsewhere on the body. On a close examination of the nails, the nail itself was seen to be separated from the nail bed. There was lack of nail bed substance. In a case of tinea involving so much of the nail, there would be involvement of the nail fold and a different discoloration than exists in this case.

DR. J. C. GRAHAM: I believe this case to be one of trophic disturbance of the nails. I see no clinical evidence of tinea. Of course, microscopic examination should be made. In onychomycosis there is usually reaction both under the nail and at the advancing margin of the lesion. This is entirely lacking in this case. An added factor against tinea is the patient's statement that the lesions of the nails have cleared up and recurred.

DR. A. WALZER: In trichophyton infection of the nail, the process usually begins at the free border and extends inward toward the root. The nail root is normal. The process in this case begins on the free border of the nail and progresses backward as in a trichophyton infection of the nail. As for treatment, I should suggest that the nails be cut off completely to the line of demarcation and that either iodine or a similar preparation be applied. The irregular distribution of the nails involved would also speak in favor of a local condition rather than a trophic distribution. Was any microscopic work done on the nail scrapings?

DR. A. M. PERSKY: How often does the ingestion of phenolphthalein produce changes in the nail?

I had a patient who had a similar condition for two years. Examination at the Post-Graduate Hospital revealed no fungi. In that case a diagnosis of drug eruption affecting the nails was made.

DR. E. A. GAUVAIN: The patient was previously treated at the Skin and Cancer Hospital, where nail scrapings were examined for ringworm and were found to be negative. The history of recovery of some of the nails does not fit in with a diagnosis of trichophytosis. She also says that these nails will almost completely recover and then other nails become involved. I thought that the condition was a dystrophy of the nails.

MYCOSIS FUNGOIDES. Presented by DR. L. J. FRANK.

S. E., a Russian, aged 77, retired, stated that twenty years before presentation a macule the size of a silver dollar developed on the left arm; the lesions became markedly thickened and enlarged peripherally. Itching was intense. After numerous roentgen treatments and applications of ointments the lesion disappeared, leaving no scar. Several similar lesions appeared on various parts of the body, and after several roentgen treatments they also cleared up.

At presentation there were scattered over the entire body infiltrated patches of various sizes, sharply outlined, some vegetative and others necrotic. Chemical examination of the blood and the Wassermann test gave negative results.

DISCUSSION

DR. M. J. CANTOR: The case is a typical one of mycosis fungoides with all varieties of lesions present, some infiltrated, some vegetative and some almost necrotic.

Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: New Orleans. Time: May 9-13, 1932.

American Dermatological Association

W. H. Mook, President, 3720 Washington Blvd., St. Louis.
W. H. Guy, Secretary, 7026 Jenkins Arcade, Pittsburgh.
Place: Havana, Cuba. Time: May 3-5, 1932.

British Association of Dermatology and Syphilology (Canadian Branch)

Philip Burnett, President, 2 Simpson St., Montreal.
L. P. Ereaux, Secretary, 1380 Sherbrooke West, Montreal.
Place: Toronto. Time: 1932.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Lee McCarthy, President, 1835 Eye St. N. W., Washington, D. C.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Howard J. Parkhurst, President, 316 Michigan St., Toledo, Ohio.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.
Place: Pittsburgh. Time: October, 1932.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
J. W. Bailey, Secretary, 10th St., and Grand Ave., Des Moines, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.
Place: Boston. Time: April 13, 1932.

Southern Medical Association, Section on Dermatology

Emmet R. Hall, Chairman, 1001 Exchange Bldg., Memphis, Tenn.
Dudley C. Smith, Secretary, University, Va.

STATE DERMATOLOGIC SOCIETIES

Louisiana Dermatological Society

R. A. Oriol, President, 921 Canal St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 150 Baronne St., New Orleans.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Edward R. Maloney, Chairman, 853 7th Ave., New York.
George C. Andrews, Secretary, 115 E. 61st St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Edward F. Corson, President, Medical Arts Bldg., Philadelphia.
Stanley Crawford, Secretary, 200, 9th St., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

MINNESOTA DERMATOLOGICAL SOCIETY

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

C. J. Woods, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

LOCAL DERMATOLOGIC SOCIETIES

ATLANTA DERMATOLOGICAL SOCIETY

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

BRONX DERMATOLOGICAL SOCIETY

Henry Silver, Chairman, 290 West End Ave., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.
B. B. Berkowitz, President, 225 Eastern Parkway, Brooklyn.

CHICAGO DERMATOLOGICAL SOCIETY

Henry E. Michelson, President, 80 S. 7th St., Minneapolis.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

H. Jerry Lavender, President, 716 Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

Howard J. Parkhurst, President, 316 Michigan St., Toledo.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

Claud W. Behn, President, 1546 David Whitney Bldg., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Chris R. Halloran, Secretary, 1052 W. 6th St., Los Angeles.

Manhattan Dermatologic Society

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Philip Burnett, President, 2 Simpson St., Montreal.
Lemuel P. Ereaux, Secretary-Treasurer, 1390 Sherbrooke St., West, Montreal.

New York Academy of Medicine, Section of Dermatology and Syphilis

Joseph J. Eller, Chairman, 100 W. 59th St., New York.
Leo Spiegel, Secretary, 241 W. 100th St., New York.

New York Dermatological Society

John Frank Fraser, President, 100 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Philadelphia Dermatological Society

Jacob M. Schildkraut, Chairman, 170 W. State St., Trenton, N. J.
Jacques P. Guequierre, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

J. H. Fiscus, Chairman, 121 N. Main St., Greensburg, Pa.
Claude B. Norris, Secretary, 244 Lincoln Ave., Youngstown, Ohio.
Place: Pittsburgh. Time: October, 1932.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Index to Current Literature

DERMATOLOGY

Actinomycosis. R. W. McQuay, Canad. M. A. J. **25**:694 (Dec.) 1931.

Articular Changes in Acrodermatitis Chronica Atrophicans. C. Hövelborn, Arch. f. Dermat. u. Syph. **164**:349 (Nov. 19) 1931; abstr., J. A. M. A. **98**:515 (Feb. 6) 1932.

Atypical Epidermophytoses. A. Matras, Arch. f. Dermat. u. Syph. **164**:291 (Nov. 19) 1931.

Bacteriophage Adaptation. P. J. Beard, J. Infect. Dis. **49**:367 (Nov.) 1931; abstr., J. A. M. A. **98**:351 (Jan. 23) 1932.

Bacteriophage in Treatment of Pyogenic Infections of Skin. L. M. Smith, Southwestern Med. **15**:509 (Nov.) 1931.

Beginning and Treatment of Dementia Paralytica and Tabes. G. Steiner, Deutsche med. Wchnschr. **57**:2007 (Nov. 27) 1931.

Behavior of Gastric Function in Dermatoses. H. Gaudig, Arch. f. Dermat. u. Syph. **164**:343 (Nov. 19) 1931.

Blue Nevus. R. Bezecny, Arch. f. Dermat. u. Syph. **164**:314 (Nov. 19) 1931.

Bullous Hemorrhagic Dermatosis in Typhoid. K. Roper, München. med. Wchnschr. **78**:2036 (Nov. 27) 1931.

Burns. G. Riehl, Jr., Arch. f. Dermat. u. Syph. **164**:409 (Nov. 19) 1931; abstr., J. A. M. A. **98**:515 (Feb. 6) 1932.

Cancer of Penis in Chinese: Fourteen Cases. S. Sato and S. Kitamura, J. Orient. Med. **15**:96 (Nov.) 1931.

Carbohydrate Metabolism in Dermatoses on Basis of Functional Tests of Liver and of Pancreas. W. Milbradt, Arch. f. Dermat. u. Syph. **164**:399 (Nov. 19) 1931.

Carcinomatous Degeneration of Rhinophyma with Remarks on Treatment of Rhinophyma. D. Eisenklam, Wien. klin. Wchnschr. **44**:1407 (Nov. 6) 1931.

Classification and Nomenclature of Atrophying or Cicatricial Alopecias and Folliculitis. E. Hoffmann, Arch. f. Dermat. u. Syph. **164**:317 (Nov. 19) 1931.

Clinical Evaluation of Various Qualities of Roentgen and Radium Rays for Treatment of Advanced Cancer. B. P. Widmann, Am. J. Roentgenol. **26**:729 (Nov.) 1931; abstr., J. A. M. A. **98**:347 (Jan. 23) 1932.

Detoxified Phenolphthalein. S. Loewe and F. Lange, Klin. Wchnschr. **10**:2217 (Nov. 28) 1931.

Education in Roentgenology for Dermatology. A. Stuhmer, Strahlentherapie **42**: 599 (Oct. 24) 1931.

Effect of Bacteriophage in Experimental Staphylococcus and Streptococcus Skin Infections. J. E. Walker, South. M. J. **24**:1087 (Dec.) 1931.

Effect of Homologous Macerated Skin on Regeneration of Epidermis. F. A. McJunkin and T. Matsui, Arch. Path. **12**:794 (Nov.) 1931; abstr., J. A. M. A. **98**:349 (Jan. 23) 1932.

Distribution of Roentgen Rays in Skin. V. Wucherpfennig, Strahlentherapie **42**:544 (Oct. 24) 1931.

Erysipelas. D. L. Richardson, Rhode Island M. J. **14**:169 (Nov.) 1931.

Filtrable and Transmissible Bacteriolytic Agents (Bacteriophage). F. W. Twort, Ann. Inst. Pasteur **47**:459 (Nov.) 1931; abstr., J. A. M. A. **98**:513 (Feb. 6) 1932.

Generalized Exanthems in Guinea-Pigs Following Sensitization with Hog Serum. P. Jordan and R. L. Mayer, Arch. f. Dermat. u. Syph. **164**:285 (Nov. 19) 1931.

Influence of Iodoform on Cultures of Streptobacillus of Soft Chancre. H. Fröhlich, Arch. f. Dermat. u. Syph. **164**:273 (Nov. 19) 1931; abstr., J. A. M. A. **98**:515 (Feb. 6) 1932.

Influence of Roentgen Rays of Various Quality on Psoriasis. G. A. Rost and P. Keller, Strahlentherapie **42**:539 (Oct. 24) 1931.

Keratoderma Blennorrhagicum: Its Histology, Clinical Characteristics, and Treatment; Eight Cases. D. Lees and G. H. Percival, Lancet **2**:1116 (Nov. 21) 1931; abstr., J. A. M. A. **98**:354 (Jan. 23) 1932.

Lesions in Lateral Horns of Spinal Cord in Acrodynia, Pellagra and Pernicious Anemia. S. T. Orton and Lauretta Bender, Bull. Neurol. Inst., New York **1**:506 (Nov.) 1931; abstr., J. A. M. A. **98**:507 (Feb. 6) 1932.

Melanoblasts in Skin Metastases of Cancer of Breast. R. Bezecny, Arch. f Dermat. u. Syph. **164**:310 (Nov. 19) 1931.

Multiple Benign Sarcoid in Organ Tuberculosis and Transformation of Lupus Vulgaris into Sarcoid. H. Schreiber, Arch. f. Dermat. u. Syph. **164**:365 (Nov. 19) 1931.

Mycosis Fungoides of Internal Organs. J. Samek and W. Feuereisen, Arch. f. Dermat. u. Syph. **164**:375 (Nov. 19) 1931.

Occupational Allergic Skin Diseases. M. Michael, Klin. Wchnschr. **10**:2223 (Nov. 28) 1931.

Origin of Light Therapy. H. Goodman, M. J. & Rec. **84**:481 (Nov. 18) 1931.

Pellagra with Special Consideration of Pellagra in Moldavia. H. Kleinmann, Arch. f. Dermat. u. Syph. **164**:393 (Nov. 19) 1931.

Penetration of Ultraviolet Rays into Live Animal Tissue. W. T. Anderson, Jr., and H. D. Fraser, Brit. J. Phys. Med. **6**:170 (Nov.) 1931.

Plastic Reconstruction of Lower Lip. E. M. Daland, New England J. Med. **205**:1131 (Dec. 10) 1931; abstr., J. A. M. A. **98**:352 (Jan. 23) 1932.

Preoperative and Postoperative Treatment of Cancer of Breast by Radiation (Metastasis Excluded). J. E. A. Lynham, Brit. J. Radiol. **4**:534 (Nov.) 1931; abstr., J. A. M. A. **98**:353 (Jan. 23) 1932.

Radiating Edge of Psoriasis Efflorescence. R. Bernhardt, Arch. f. Dermat. u. Syph. **164**:334 (Nov. 19) 1931.

Radiation Treatment of Some Skin Affections. E. M. Henry, Canad. M. A. J. **25**:702 (Dec.) 1931.

Relations Between Skin Pigmentation and Elimination of Bilirubin and of Biliverdin in Urine During Icterus. K. Franke, Ztschr. f. d. ges. exper. Med. **79**:125 (Oct. 20) 1931.

Relations of Color of Hair and Skin to Skin Epithelioma. S. Epstein, Arch. f. Dermat. u. Syph. **164**:304 (Nov. 19) 1931.

Secondary Carcinoma of Skin. A. Matras, Wien. klin. Wchnschr. **44**:1408 (Nov. 6) 1931.

Roentgen Carcinoma as Result of Irradiation Therapy. H. Holthusen and K. Englmann, Strahlentherapie **42**:514 (Oct. 24) 1931.

"Smallpox-Like" Case of Eczema Vaccinatum with Subsequent Generalized Vaccinia. M. Kaiser and G. Blass, Arch. f. Dermat. u. Syph. **164**:357 (Nov. 19) 1931.

Specific Action of Intracutaneous Injection. Wolynskij and Stoljarova, Ztschr. f. d. ges. exper. Med. **79**:164 (Oct. 20) 1931; abstr., J. A. M. A. **98**:359 (Jan. 23) 1932.

Total Irradiation with Roentgen Rays. F. M. Groedel and H. Lossen, Strahlentherapie **42**:532 (Oct. 24) 1931.

Treatment of Dermatophytosis. P. E. Bechet, New York State J. Med. **31**:1456 (Dec. 1) 1931.

Treatment of Roentgen Injuries with Rays of Long Wavelengths. W. Brocker, Strahlentherapie **42**:551 (Oct. 24) 1931; abstr., J. A. M. A. **98**:358 (Jan. 23) 1932.

Twort Phenomena and Bacteriophage. F. d'Hérelle, Ann. Inst. Pasteur **47**:470 (Nov.) 1931.

Ulerythema Ophryogenes and Its Relations to Congenital Keratosis Pilaris. O. Dittrich, Arch. f. Dermat. u. Syph. **164**:383 (Nov. 19) 1931.

Volatile Oils as Cause of Allergic Disturbances of Skin and of Mucous Membrane. E. Urbach and C. Wiethe, München. med. Wchnschr. **78**:2030 (Nov. 27) 1931; abstr., J. A. M. A. **98**:516 (Feb. 6) 1932.

SYPHILOLOGY

Acetarsone in Treatment of Syphilis in Children: Its Dosage. A. Bratusch-Marrain, Wien. klin. Wchnschr. **44**:1380 (Oct. 30) 1931.

Agranulocytic Angina Due to Arsphenamine. G. Delpiano, Riforma med. **47**:1669 (Nov. 2) 1931; abstr., J. A. M. A. **98**:355 (Jan. 23) 1932.

Agranulocytosis Following Treatment with Neoarsphenamine. E. Essenfeld, München. med. Wchnschr. **78**:2034 (Nov. 27) 1931; abstr., J. A. M. A. **98**: 516 (Feb. 6) 1932.

Combined Simultaneous Arsenobenzene Bismuth Therapy: Report of 102 Patients with Early and Late Syphilis. T. D. Rhodes, J. Indiana M. A. **24**:606 (Nov. 15) 1931.

Laboratory Diagnosis of Syphilis. J. A. Kolmer, Southwestern Med. **15**:523 (Nov.) 1931.

Precipitation Test for Syphilis: Influence of Diluents of Antigen on Intensity of Flocculation. E. Weiss, J. Infect. Dis. **49**:436 (Nov.) 1931; abstr., J. A. M. A. **98**:351 (Jan. 23) 1932.

Syphilis of Liver in Adults. D. D. Yablokov, Trudi tomskogo cossud med. inst. **1**:113 (Nov. 2) 1931.

Treatment of Neurosyphilis, Other Than Paresis, with Malaria. A. Paige, R. J. Rickloff and E. D. Osborne, New York State J. Med. **31**:1441 (Dec. 1) 1931; abstr., J. A. M. A. **98**:352 (Jan. 23) 1932.